The One-Electron Oxidation of Metalloporphyrins

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Abstract: Many metalloporphyrins can be reversibly oxidized in a one-electron step. The midpoint oxidation potentials of magnesium octaethylporphyrin (MgOEP), ZnOEP, CuOEP, NiOEP, and PdOEP were found to be approximately 427, 525, 601, 636, and 725 mV *vs.* saturated calomel electrode in methanol or chloroform–methanol. Plots of E_1 *vs.* log (Ox/Red) were 59 ± 3 mV, indicating a one-electron oxidation. The order of the oxidation potentials increases with the qualitative stability constants of the porphyrin complexes and also with the electronegativity values of the metal ions. The stannic dication (Sn(IV)OEP diacetate) and the diprotonated dication ($OEPH_4^{2+}$) porphyrins were resistant to potentials greater than 1 V. A simple electrostatic argument can explain the reduction and oxidation behavior of these and other porphyrin derivatives. The more negative is the porphyrin ring, the easier it is to remove an electron, and *vice versa.* Bacteriochlorophyll gave a one-electron titration curve with a midpoint of 270 mV. Chlorophyll was changed to a different chlorin which itself had a midpoint potential of ~550 mV. Optical and esr spectra of the resulting radicals are reported.

The redox properties of the iron porphyrins or hemes have been extensively investigated because of their revelance to respiration in biological systems. The one-electron oxidation–reduction of the iron atom and the influence of other ligands on these potentials have been well characterized.[1] The various valence states of manganese[2] porphyrins have also been described. However, the usefulness of the tetrapyrrole macrocycle in energy transfer in biological systems is not restricted to the modification of metal ion redox potentials. The porphyrin macrocycle itself can be easily and reversibly reduced and oxidized. This is probably of importance in the action of chlorophyll and bacteriochlorophyll during the conversion of light to chemical energy in photosynthesis. Chlorophyll (and bacteriochlorophyll) may be ubiquitous in photosynthetic organisms not only because they can absorb sunlight effectively, but also because the macrocycle can release and take up electrons as easily and reversibly as an inorganic ion.

The reduction[3] and photoreduction[4] of porphyrins and chlorins and their metallo derivatives to phlorin-type pigments have been investigated and some polarographic reduction potentials are known.[5,6] The reversible oxidation of chlorophyll,[7,8] bacteriochlorophyll,[8] and Mg tetrabenzporphin[8] has been reported but no conclusions relating to the structure of the oxidation products have been reached. Stanienda has reported the polarographic oxidation potentials of free and various metal porphyrins[9] and of chlorophylls.[10] The one-electron oxidation of various metal chelates of the phthalocyanines has also been reported,[11] the metal derivatives being more stable than the free base.

We have found that the stability of the oxidized metalloporphyrins is dependent on the solvent and that both the ease of oxidation and the localization of the electron depend on the metal ion.. Under well-defined conditions the one-electron oxidation of the metalloporphyrins is strikingly clean and reversible.

Experimental Section

A. Preparation of the Metalloporphyrins. Magnesium octaethylporphyrin (MgOEP) was prepared by a variant of the method of Baum, Burnham, and Plane.[12] OEP[13] (950 mg) was dissolved in 100 ml of pyridine (Mallinckrodt AR); 5 g of anhydrous $Mg(ClO_4)_2$ was added, and the solution was gently refluxed for 18 hr in the dark. The pyridine solution was diluted with 1 l. of peroxide-free ether and washed five times with 250 ml of one-tenth saturated sodium acetate solution. The ether solution was evaporated under vacuum to 80 ml and cooled to −30°. The resulting crystals were filtered off (500 mg), the solution was further concentrated (40 ml), and another 350 mg of crystalline material was collected after standing in the cold. The crystals were dried under vacuum at 60°.

Anal. Calcd for MgOEP·2Py($C_{46}H_{54}N_6Mg$): C, 77.25; H, 7.60; N, 11.72. Found: C, 77.24, 76.92; H, 7.79, 7.92; N, 11.76, 11.56.

The pyridine-free compound was prepared by dissolving 60 mg of the above pyridine complex in 300 ml of peroxide-free ether and washing six times with about 200 ml of 0.1 *N* HCl, then with 100 ml of saturated $NaHCO_3$ solution and three times with 200 ml of water. The ether was evaporated and the residue recrystallized from benzene–petroleum ether (30–60°).

Anal. Calcd for MgOEP (557.1) $C_{36}H_{44}N_4Mg$: C, 77.26; H, 7.95; N, 10.02. Found: C, 76, 71; H, 7.90; N, 9.94.

This pyridine-free compound did not crystallize as well as the pyridine complex but behaved exactly like it on oxidation. This is because the pyridine complex is completely dissociated, as shown by spectral measurements, at the concentrations used, about 10^{-5} *M.* Because of the ease with which the oxidation occurred in simple alcohols compared to many other solvents, the absorption spectra of both MgOEP and the pyridine complex were taken in pyridine, benzene, dimethyl sulfoxide, butanol, methanol, and petroleum ether in order to see if in alcohol special species of the porphyrin, *e.g.*, dimers, were formed. The data showed that the wavelength of the Soret band increases with increasing refractive index of the solvent, as is expected for an allowed transition. The visible bands are far less affected, again as expected for weak transitions. The absorbancy indexes show a variation of only ±5%, some of which

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[1] J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier Publishing Co., New York, N. Y., 1964, p 67 ff.

[2] M. Calvin, *Rev. Pure Appl. Chem.*, **15**, 1 (1965).

[3] R. B. Woodward, *Ind. Chim. Belges*, 1293 (1962); G. L. Closs and L. E. Closs, *J. Am. Chem. Soc.*, **85**, 818 (1963); H. H. Inhoffen, P. Jäger, R. Mählhop, and C. D. Mengler, *Ann. Chem.*, 704, 188 (1967).

[4] D. Mauzerall, *J. Am. Chem. Soc.*, **84**, 2437 (1962).

[5] D. W. Clack and N. S. Hush, *ibid.*, **87**, 4238 (1965).

[6] R. H. Felton and H. Linschitz, *ibid.*, **88**, 1113 (1966).

[7] For a recent publication with references to earlier work, see B. Diehn and G. R. Seely, *Biochim. Biophys. Acta*, **153**, 862 (1968).

[8] J. C. Goedheer, *Photochem. Photobiol.*, **6**, 521 (1967); J. C. Goedheer in "The Chlorophylls," L. P. Vernon and G. R. Seely, Ed., Academic Press, New York, N. Y., 1966, p 165 ff.

[9] A. Stanienda and G. Bieble, *Z. Physik. Chem.* (Frankfurt), **52**, 254 (1967).

[10] A. Stanienda, *Z. Physik. Chem.* (Leipzig), **229**, 257 (1965).

[11] A. E. Cahill and H. Taube, *J. Am. Chem. Soc.*, **73**, 2847 (1951); P. George, D. J. E. Ingram, and J. E. Bennett, *ibid.*, **79**, 1870 (1957).

[12] S. J. Baum, B. F. Burnham, and R. A. Plane, *Proc. Natl. Acad. Sci. U. S.*, **52**, 1439 (1964).

[13] H. H. Inhoffen, J.-H. Fuhrhop, H. Voigt, and H. Brockmann, Jr., *Ann. Chem.*, **695**, 133 (1966).

Table I

Compd	Oxidant	Solvent[a]	Ratio of oxidant to oxidized porphyrin[b]	Remarks
MgOEP	I_2	MeOH	2	Stable
MgOEP	$Fe(ClO_4)_3$	MeOH	2	Gave most stable potentials
MgOEP	NBS[c]	MeOH	1	Oxidized the 683 product further at high oxidant:porphyrin ratios
MgOEP	DCCB[d]	MeOH	3	Gave unstable potentials, potentials fell off after midpoint
ZnOEP	$Fe(ClO_4)_3$	MeOH	4	Stable
	NBS[c]	MeOH	1	Gave additional compound with absorption at 620 nm
CuOEP	$Fe(ClO_4)_3$	$CHCl_3$–MeOH (4:1)	10	Stable
	NBS[c]	$CHCl_3$–MeOH (4:1)	3	Unstable potential
NiOEP	$Fe(ClO_4)_3$	$CHCl_3$–MeOH (4:1)	40	Stable
PdOEP	$Fe(ClO_4)_3$	$CHCl_3$–MeOH (4:1)	60	Stable
Fe(III)OEP-OH	NBS[c]	$CHCl_3$–MeOH (1:5)	10	Irreversible
OEP H_2^{2+}	NBS[c]	MeOH + 5% H_2SO_4	100	No immediate oxidation
Sn(IV)OEP$(OAc)_2$	NBS[c]	MeOH	>100	No reaction at all
BChl	I_2	MeOH	1	Stable
Chl[a]	$Fe(ClO_4)_3$	MeOH	20	Could not be titrated directly; only the return of a different chlorin coupled with the decay of the potential could be followed; this chlorin could then be oxidized and reduced

[a] Omitted here are salts (LiCl, $LiClO_4$) usually added to buffer salt effects during the titration. [b] At the midpoint of the oxidation; when no oxidation occurred, the added excess of oxidant is stated. [c] NBS = N-bromosuccinimide. [d] DCCB = dichlorodicyanobenzoquinone.

is experimental error. The spectrum in methanol is in no way singular. This does not strictly rule out aggregation since it is possible in exceptional cases to form such species with little interaction of the transition dipole moments.

Zn, Pd, Cu, and Ni complexes were obtained in the usual way (see ref 1), which will not be described here. Bacteriochlorophyll and chlorophyll were also obtained by standard procedures.[14] Sn(IV)OEP diacetate was prepared by refluxing OEP with $SnCl_2$ in acetic acid, oxidizing with air, and crystallizing from acetic acid. Fe(III)OEP hydroxide was obtained by refluxing OEP and Fe$(ClO_4)_2 \cdot 6H_2O$ in pyridine for 10 min, oxidizing with air, and crystallizing from benzene (*Anal.* Calcd for $C_{36}H_{45}N_4OFe$ (605.7): C, 71.39; H, 7.44; N, 9.25. Found: C, 71.34; H, 7.29; N, 9.07).

Ca-, Sr-, Ba-, and CdOEP solutions were also prepared by Baum's[12] method from the corresponding perchlorates. Ca- and CdOEP could be crystallized from $CHCl_3$–MeOH; Sr- and BaOEP demetalized immediately in methanol.

The completion of complex formation was always checked before the beginning of the work-up procedure by examining the solutions in the hand spectroscope for the complete disappearance of the 620 OEP band.

B. Spectra. Absorption measurements were made on a Cary Model 14R spectrophotometer with appropriate slit widths and scanning speeds. The spectra shown in Figures 2–6 were obtained at a pigment concentration of about 3×10^{-5} *M* and an oxidant concentration of 10^{-3} *M* except for PdOEP, 10^{-2} *M*. The near-infrared and visible regions of the spectrum were scanned with the lead sulfide detector to locate bands invisible in the hand spectroscope. The latter instrument was invaluable for preliminary experiments.

Esr Measurements. These were performed at a frequency of about 9 KMc on both a Varian model and a superheterodyne[15] spectrometer both using 100-Kc modulation. Most of the quantitative data were obtained on the former, and the *g* values and low-temperature experiments on the latter. Flat thin cells were used to minimize microwave power losses. The resonances did not saturate with microwave power at the levels used. Line widths were determined from the peak to peak spread and the modulation amplitude was reduced until its effect on line width was negligible (<5%). Measurements on both spectrometers agreed. The *g* values were determined by sweeping both increasing and decreasing magnetic field to average out various hysteresis effects. The field was calibrated by measuring the proton magnetic resonance frequency at a precalibrated position adjacent to the cavity. Both this frequency and the microwave frequency were measured with electronic counters. Diphenylpicrylhydrazyl was used both as a check on our *g* measurements (measured and literature[16] value 2.0036) and as a calibration standard for determining the number of spins in the cavity. It was diluted in the same solvent used for the porphyrins to keep the *Q* of the cavity constant. Sample positioning was controlled by observing the cavity resonance. Because of the complex line shape of the DPPH, the area of the differential esr signal was used for the comparison with proportional correction for different line widths. Allowances were made for varying modulation amplitudes, amplifier gains, and magnetic field sweeps. A check was run by also using double integration of the esr signal (independent of line width) and amplitude of smoothed signal (proportional to square of line width). The agreement was ±20%.

The line widths of esr spectra of the zinc and magnesium porphyrin radicals measured in the presence of air were somewhat broader than in the absence of oxygen. The data quoted in Table III refer to deoxygenated solutions. Concentrations of the radicals were usually 10^{-5} to 10^{-4} *M*.

Correlation of optical and esr spectra was accomplished by oxidizing a sample of the metalloporphyrin, using one aliquot for the esr spectrum and one for the optical spectra. The fraction oxidized was varied by varying the amount of oxidant, and the totally oxidized solution was reversed by adding a suitable reductant such as triethylamine.

C. Oxidation Procedure. General Procedure. The porphyrin solutions (10 ml, 3–10 $\times 10^{-5}$ *M*) were placed in a 1-cm cuvette of Pyrex glass with a 10 cm long and 3 cm wide neck. This tube was topped by a 29/40 ground joint which held a three-hole rubber stopper with gas inlet tube, titrant inlet tube, and sce|Pt combination electrode with a ceramic junction (Radiometer Pk 149 used with radiometer pH meter type 4). Another assembly had a fourth hole and a platinum electrode was introduced there; the potential was measured against a fiber junction calomel electrode (Beckman 39178 used with Beckman Model G pH meter). The oxidant was added through a thin Teflon tube by a syringe microburet Model No. S B2, Micro-metric Instrument Co. with an 0.2-ml syringe. Another Teflon tubing led to the bottom of the cuvette, and argon was bubbled through the solution to deoxygenate it and mix it with added oxidant. This tubing was the inner tubing of a coaxial set; the outer tube was flushed with argon, thus isolating the former from air. The whole assembly was sealed up with tape, placed

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(14) H. H. Strain and W. A. Svec, "The Chlorophylls," L. P. Vernon and G. R. Seely, Ed., Academic Press, New York, N. Y., 1966, p 53; A. F. H. Anderson and M. Calvin, *Nature*, **194**, 285 (1962); H. J. Perkins and D. W. A. Roberts, *Biochim. Biophys. Acta*, **58**, 486 (1962).

(15) G. Feher, *Bell Syst. Tech. J.*, **36**, 449 (1957).

(16) M. S. Blois, Jr., H. W. Brown, and J. E. Maling, Neuvieme Collique Ampere Librairie Payot, Geneva, 1960, p 243.

Table II. Midpoint Potentials of Metalloporphyrins

Compound[a]	Potential, mV	Slope[b]	Remarks
Bacteriochlorophyll[c]	270 ± 10	64	Fully reversible
Mg octaethylporphyrin[c,d]	427 ± 5	60	Fully reversible
Zn octaethylporphyrin[d]	525 ± 10	59	Fully reversible
Chlorin (chlorophyll)[c]	550 ± 50		Reversible to chlorin
Cu octaethylporphyrin[e]	601 ± 10	60	Fully reversible
Ni octaethylporphyrin[e]	636 ± 15	54	Fully reversible
Pd octaethylporphyrin[f]	726 ± 15	56	Fully reversible
Fe(III) octaethylporphyrin hydroxide[c]	>840		Irreversible
H_2 octaethylporphyrin dication[g]	>1000		Slowly destroyed by large excess of NBS
Sn(IV) octaethylporphyrin diacetate[c]	>1100		Completely stable against NBS in MeOH

[a] All the solutions were in the concentration range 10^{-4}–10^{-5} M and at 23 ± 2°, constant to <1° during a titration. [b] Slope in millivolts per unit log (Ox/Red); error ≤5%. [c] In MeOH. [d] In MeOH and 10^{-2} mol in $LiClO_4$. [e] In $CHCl_3$–MeOH (4:1). [f] $CHCl_3$–MeOH (4:1) and 10^{-2} mol in $LiClO_4$. [g] In MeOH + 5% H_2SO_4.

in the cell compartment of a Cary Model 14 spectrophotometer, and covered with a metal box. After each addition of oxidant, 1 min was allowed for the potential and the absorption changes to stabilize. The argon stream was cut off during measurement of the spectra.

The concentration of the added methanolic oxidant solutions was usually 10^{-2} M. In the cases of Cu-, Ni-, and PdOEP, when a large excess of oxidant was needed, 10^{-1} M solutions were used. The added volume never exceeded 2% of the total volume. The solutions of the oxidants in methanol were always freshly prepared immediately before the titration. The pigment solution usually contained 10^{-2} M $LiClO_4$. Table I gives the compounds oxidized, the oxidants, and a rough estimate of the ratio moles of compounds to moles of oxidized porphyrins at the half-oxidation point. The ratio of oxidized to reduced form required for the plots of Figure 1 and Table II were obtained from the spectral measurements. The use of a single absorption band of either the porphyrin or oxidized porphyrin or a combination of the two gave the same ratio within experimental error.

The use of two different calomel electrodes caused a uniform shift of 10 mV in the measured potentials. The Beckman electrode gave the higher potential. We explain this by the assumption of different diffusion potentials between the KCl bridge and the methanol solution; the Beckman electrode has a fiber junction, the Radiometer electrode a ceramic plate. We thus subtracted 10 mV from all potentials measured with the Beckman electrode. Some comments about the solvents used follow.

MgOEP. The oxidized species was particularly stable in simple alcohols. In *t*-butyl alcohol the maximum was at 663 nm instead of 683 nm, and iodine could not oxidize MgOEP in this solvent. On dilution of the methanol solutions with other solvents such as dimethylformamide, acetone, ether, petroleum ether, pyridine, and benzene, the starting material was gradually re-formed. Chloroform had less effect. Addition of up to 20% water did not cause any obvious change in the oxidation product. A large excess oxidant in any of these solvents destroyed the porphyrin irreversibly. Oxidation with ferric perchlorate or with iodine, which have different acidities in methanol, gave the same midpoint potential. Addition of protons equivalent to the MgOEP concentration did not change the potential of a partially oxidized solution. Under conditions where 2% of protons equivalent to MgOEP could have been detected with a glass electrode, no increase in acidity was noted on oxidizing MgOEP with iodine.

ZnOEP. The effects of solvents were similar to that of MgOEP. The ZnOEP is far less soluble in methanol than is MgOEP.

CuOEP, NiOEP, and PdOEP. Because of low solubility in methanol these complexes were oxidized in chloroform–methanol (4:1).

Ca-, Sr-, Ba-, and CdOEP. Ca- and CdOEP were dissolved in methanol and titrated as described with $Fe(ClO_4)_3$ or I_2 or dichlorodicyanobenzoquinone. In every case the metal complex decomposed gradually and a spectrum ascribable to the monoprotonated porphyrin was observed. No oxidation product could be found. Sr- and BaOEP could not even be dissolved in methanol without decomposition.

Electrophoresis of Oxidized Metalloporphyrins. A spot of the green oxidation product of MgOEP on paper electrophoresis in the presence of excess oxidant moved to the cathode, before it decomposed to a mixture of OEP and MgOEP. The oxidation products of Cu-, Ni-, and PdOEP also moved to the cathode on free electrophoresis. The migration of the front could be reversed by changing the sign of the applied field.

Temperature Dependence of the Spectrum of the Oxidation Products. ZnOEP, 2 × 10^{-5} M, in MeOH-10% $CHCl_3$ was fully oxidized with ~6 × 10^{-4} M $Fe(ClO_4)_3$; a spectrum with bands at 950, 655, 575, 389, and 358 nm appeared (Figure 6). The reaction mixture was then cooled in a glass dewar with acetone–Dry Ice and the spectrum taken at the temperature of the cooling bath. The long-wavelength band more than doubled in intensity, and the 655-nm band disappeared (Figure 6) along with the band at 389 nm. After standing for some minutes at room temperature the original spectrum was completely restored. On heating to ~60°, the 655- and 389-nm bands increased and the others disappeared. This also was reversed on cooling to room temperature. The narrow esr signal (Table III) is associated with the 655- and 389-nm absorptions as shown by loss of the resonance at −60°. About one-half to one-third of the radical is present at −10° as at 20°.

Table III. Esr Spectra of Oxidized Metalloporphyrins[a]

Metal complex of octaethylporphyrin	*g*	Line width, G
Mg	2.0027	3.8
Zn	2.0025	2.7
Cu (before oxid)	~2.1 (anisotropic)	~150
Ni	2.0020	3.6
Pd	1.9991	3.6
Bacteriochlorophyll	2.0025	12.6

[a] Experimental conditions similar to those used for absorption spectra; temperature 25° except Ni and Pd −50°. Error in g = ±0.0002; error in ΔH = ±5%.

The absorption spectra of the oxidized nickel and copper species are also temperature dependent. The visible spectrum broadens at low temperature and new bands at 880 and 895 nm, respectively, appear. The oxidized magnesium species is partially converted to a species absorbing at 940 nm at Dry Ice temperatures, but only at high concentrations (5 × 10^{-4} M).

Results and Discussion

The one-electron oxidation products of the metalloporphyrins are highly reactive species, having redox potentials between those of iodine and bromine (Table II). They are thus susceptible to reaction with the surrounding medium and to further oxidation leading, finally, to ring opening and bile pigment formation. We had previously[17] explained the stabilizing effect of simple alcoholic solvents on the oxidation of magnesium octaethylporphyrin as caused by nucleophilic attachment to the bridge methine carbon of the radical cation with concomitant release of a proton. However, we

[17] J.-H. Fuhrhop and D. Mauzerall, *J. Am. Chem. Soc.*, 90, 3875 (1968).

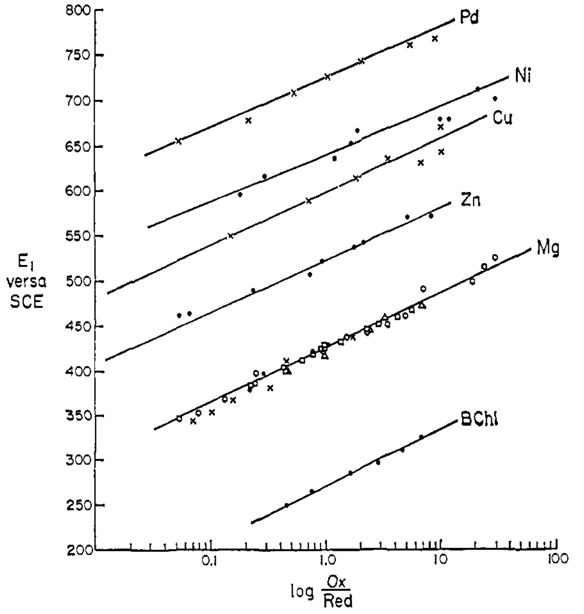

Figure 1. Plot of E_1 *vs.* log (Ox/Red) of some metalloporphyrins and bacteriochlorophyll. Oxidants: CuOEP, NiOEP, ZnOEP, PdOEP: $Fe(ClO_4)_3$; BChl: I_2; MgOEP: ○, $Fe(ClO_4)_3$; ×, dichlorodicyanobenzoquinone; □, I_2; ●, I_2, reverse titration with I^-; △, N-bromosuccinimide. Pigment concentration $\sim 3 \times 10^{-5}$ *M.*

have not been able to obtain evidence for this structure. The green species moves as a cation on electrophoresis and the potential appears to be independent of acidity or of the anion present. Felton, *et al.*,[18] have observed a similar species on electrochemical or chemical oxidation of magnesium octaethylporphyrin in methylene chloride. Their claim that this species is the simple cation is based on a partially resolved nine-line esr signal of zinc tetraphenylporphyrin (and more recently[19] of the magnesium derivative), and on "agreement between the calculated and observed electronic absorption spectra of the cation radicals." Our point is that electronic spectra as different as those of the magnesium derivative (Figure 2) and of the copper (Figure 3), nickel (Figure 4), and palladium (Figure 5) complexes cannot possibly be caused by the same electronic species. The complexity of the spectra of the zinc complex(es) (Figure 6) underlines this point. Felton[19] has suggested that because of the closeness of the two highest filled orbitals in the porphyrin, slight changes caused by the metal ion or solvent would allow the hole in the oxidized species to occupy either of these orbitals. This would result in changes in optical and esr spectra. Our data are compatible with such a description. However, the contribution from distortions of the macrocycle and from aggregates and ion complexing remain to be determined. We shall discuss each metalloporphyrin in turn, followed by a general discussion of their redox properties and some comments on the allied biological pigments.

Magnesium Porphyrin. The oxidation of magnesium octaethylporphyrin was studied in detail because of its interest as the simplest model of chlorophyll oxidations. Some of the results have been outlined previously.[17]

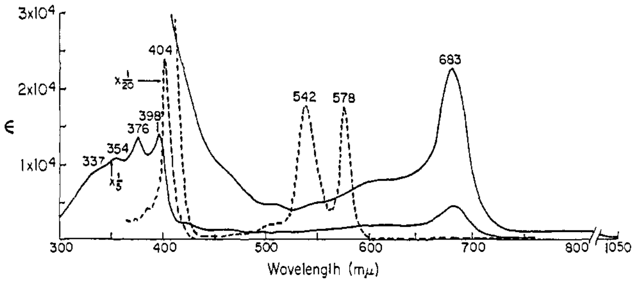

Figure 2. Absorption spectra of magnesium octaethylporphyrin (— — —) and its oxidation product (———); solvent: methanol; oxidant: ferric chloride.

The potentials obtained on titrating the magnesium porphyrin with various oxidants are shown in Figure 1. The slope of this line identifies the reaction as a one-electron oxidation with a midpoint potential of 427 mV (Table II) *vs.* saturated calomel electrode in the particular solvent used. The ratio of oxidized to reduced form was calculated from simultaneous spectral measurements. The use of various absorption bands led to the same points, within experimental error. The absorption spectrum is shown in Figure 2. The independence of the potentials from the oxidant confirms that it is the porphyrin-oxidized species that causes the potential change. A reverse titration with potassium iodide as reductant confirmed the reversibility of the system. The midpoint potential was the same at 10^{-5} to 10^{-4} *M* MgOEP concentration, but decreased ~ 20 mV at 5×10^{-4} *M*, indicating onset of aggregation.

In confirmation of the potentiometric results, the expected esr signal of the oxidized product was found to account quantitatively ($\pm 20\%$) for the porphyrin present in the solution. The *g* value of the radical, 2.0027, is similar to that observed in other porphyrin radicals,[6,20] and also to that seen in aromatic anions and cations.[16,21] The *g* value seems to be only slightly affected (± 0.0002) by the odd electron being in an anionic (reduced) radical or a cationic (oxidized) radical. This presumably reflects the simple π orbitals occupied by the electron and the small spin–orbit coupling of an electron on a carbon or nitrogen nucleus. The gaussian line shape suggests a large number of unresolved hyperfine lines caused by interaction with protons and nitrogen nuclei. Under certain conditions, in fact, at least five lines, with a separation of 1.5 G, were distinguished. The rather narrow line width suggests that considerable electron density occurs on carbons containing no protons. Since the line width remained constant down to 10^{-5} *M*, it is unlikely to be affected by electron or spin exchange. There was no change in the esr signal on cooling to $-50°$.

Copper, Nickel, and Palladium Porphyrins. These transition-metal chelates differ from the magnesium chelates by the presence of electrons in d orbitals. Because of the strong interaction between the electrons in these orbitals and those on the nitrogen atoms of the porphyrin ring, their exact energy level is strongly dependent on both their degree of occupancy and on the identity of ligands in the fifth and sixth positions.

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(18) R. H. Felton, D. Dolphin, D. C. Borg, and J. Fajer, *J. Am. Chem. Soc.*, **91**, 196 (1969).

(19) R. H. Felton, personal communication.

(20) D. Mauzerall and G. Feher, *Biochim. Biophys. Acta*, **79**, 430 (1964).

(21) B. Segal, M. Kaplan, and G. K. Fraenkel, *J. Chem. Phys.*, **43**, 4191 (1965).

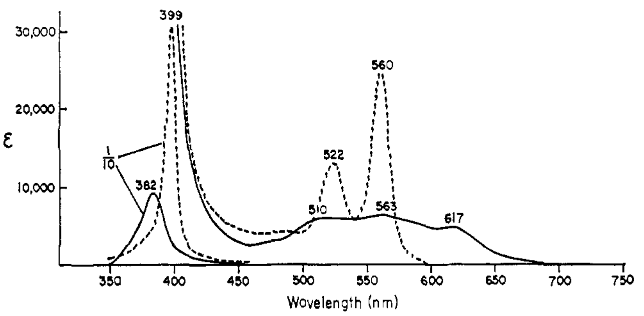

Figure 3. Absorption spectra of copper octaethylporphyrin (— — —) and its oxidation product (———); solvent: chloroform–methanol, 4:1; oxidant: ferric perchlorate.

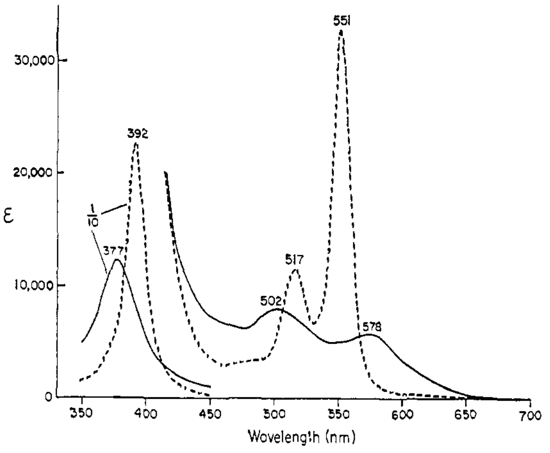

Figure 4. Absorption spectra of nickel octaethylporphyrin (— — —) and its oxidation product (———); solvent: chloroform–methanol, 4:1; oxidant: ferric perchlorate.

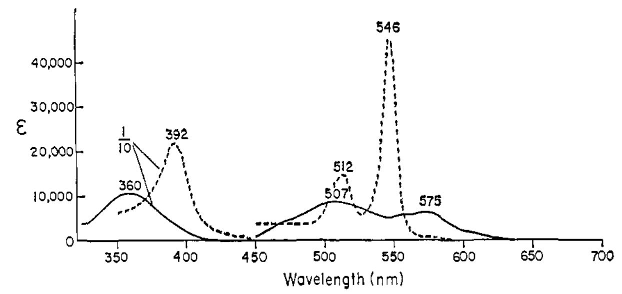

Figure 5. Absorption spectra of palladium octaethylporphyrin (— — —) and its oxidation product (———); solvent: chloroform–methanol, 4:1; oxidant: ferric perchlorate.

Zerner and Gouterman[22] have estimated the positions of these d-orbital levels with respect to the π levels for transition metal porphyrins with no ligands in the fifth and sixth positions. Since methanol is a medium-field ligand[23] and the only anion present in this system is perchlorate, these calculations are at least a first approximation to our experimental conditions. They show the filled, completely paired lower four d orbitals of Ni to be somewhat above the filled π levels; the half-filled ($d_{x^2-y^2}$) orbital of Cu to be far above the filled π levels, close to the lowest empty degenerate porphyrin π levels; and the Zn highest filled orbital ($d_{x^2-y^2}$) to be between the filled and empty porphyrin π orbitals.

The removal of an electron from these metalloporphyrins will thus largely involve orbitals on the metal ion. However, once the electron is removed, the energy level of the d orbitals will decrease more than that of the π orbital levels[24] because the former orbitals are far more localized. This leaves the hole in the π orbital in the case of nickel and, very likely, palladium. In the case of copper, the large separation of the $d_{x^2-y^2}$ and filled π orbitals suggests that the original order may be conserved. The case of zinc appears to be borderline (see below). The absorption and esr spectra support these qualitative considerations. The absorption spectra of the copper (Figure 3), nickel (Figure 4), and palladium (Figure 5) chelates are very similar and resemble porphyrins far more than that of the magnesium chelate (Figure 2). The ratio of intensities of Soret to visible transitions is 10 or 20 to 1, as it is in porphyrins. The dipole strength of the allowed Soret transitions is reduced on oxidation, as is predicted for the nickel and palladium porphyrins. The esr spectra of the oxidation products are in good agreement with these views (Table III). The broad anisotropic signal of the copper porphyrin (similar to that of monomeric copper uroporphyrin observed by Blumberg and Peisach[25] and of copper etioporphyrin observed by Roberts and Koski[26]) vanishes on oxidation and no other esr signal was detectable (maximum ΔH detectable, 200 G; H_0 swept from $g = 1.1$ to $g = 8.7$). This result agrees with simple removal of the unpaired electron from the d orbital, leaving a diamagnetic, nominally Cu^{3+} porphyrin complex. This point could be verified by measurement of the magnetic suspectibility or nmr spectrum. This would rule out the possibility of the presence of two unpaired electrons, one in the ring and one on the copper, giving a highly anisotropic, and thus very broad, esr spectrum. The nickel porphyrin initially shows no esr spectrum (maximum ΔH detectable 50 G, H_0 swept from $g = 1.1$ to $g = 8$). The absorption spectrum also corresponds to a diamagnetic species as observed by McLees and Caughey,[27] for nickel etioporphyrin. Strong field ligands, *e.g.*, piperidine, were found to reduce the separation of the d orbitals and allow formation of the paramagnetic species which absorb at longer wavelengths. On oxidation of NiOEP with $Fe(ClO_4)_3$, the product gives an esr signal of width 3.6 G (Table III). This is rather narrow for an electron in a d orbital, and together with the g value 2.0020, close to that of the free electron, strongly suggests that the electron is largely in a π orbital. The palladium derivative should be very similar to that of the nickel complex. Again the initial compound shows no detectable esr spectrum (maximum ΔH and g sweep as for nickel chelate), and the oxidized product has an esr spectrum of line width 3.6 G and g = 1.9991. The markedly lower g value is undoubtedly caused by increased spin–orbit coupling by the heavy metal atom. Both the sign and the magnitude of the effect again support π orbital occupancy of the spin.

The quoted g values and line widths refer to a solution of the Ni and Pd pigments oxidized with ferric ion, at -50°.

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(22) M. Zerner and M. Gouterman, *Theoret. Chim. Acta*, **4**, 44 (1966).

(23) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 2nd ed, Interscience Publishers, New York, N. Y., 1966, p 680.

(24) M. Zerner, M. Gouterman, and H. Koboyashi, *Theoret. Chim. Acta*, **6**, 363 (1966).

(25) W. E. Blumberg and J. Peisach, *J. Biol. Chem.*, **240**, 870 (1965).

(26) E. M. Roberts and W. S. Koski, *J. Am. Chem. Soc.*, **82**, 3006 (1960).

(27) B. D. McLees and W. S. Caughey, *Biochemistry*, **7**, 642 (1968).

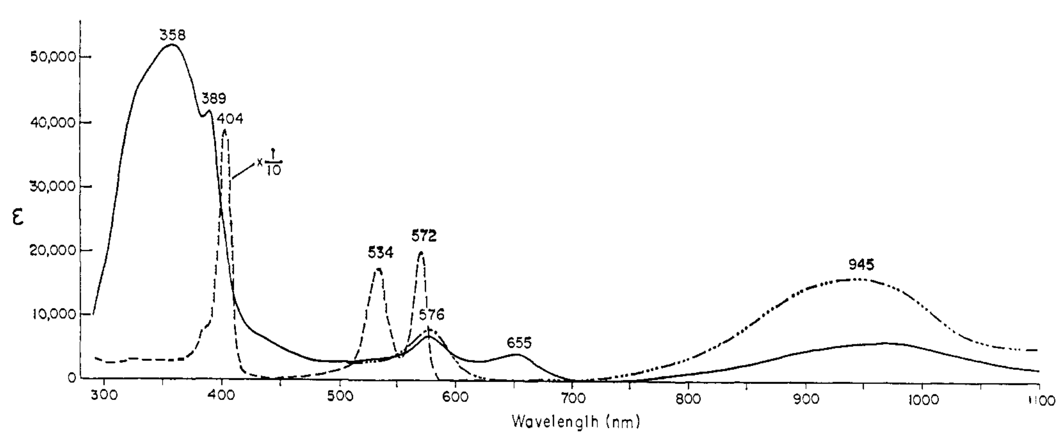

Figure 6. Absorption spectra of zinc octaethylporphyrin (— — —); its oxidation product at room temperature (———) and after cooling to Dry Ice–acetone temperature (— · · —); solvent: methanol–chloroform, 10:1; oxidant: ferric perchlorate.

The line shape is gaussian. At room temperature and above the line widths are about 10 G, the *g* values are about 0.05% higher, and the line shape is closer to Lorentzian. Thus, the resonances appear to be lifetime broadened at the higher temperatures with an exchange time of less than 10^{-8} sec.

Zinc Porphyrin. The oxidation of the zinc chelate is somewhat more complicated. We would expect to lose the electron from the highest filled $d_{x^2-y^2}$ orbital, leaving a situation similar to the divalent copper derivative, but with much lower energy d levels. In fact, the optical spectra (Figure 6) of the oxidized species is rather complex, suggesting two components. On lowering the temperature, one form predominates. It absorbs in a very broad band at 950 nm, a weak band at 575 nm, and a Soret band at 358 nm. At high temperatures, the other form absorbing at 655 and 389 nm predominates. The narrow esr signal ($\Delta H = 2.7$ G, $g = 2.0025$, Table III) is associated with the 655 and 389 nm absorptions as shown by loss of the magnetic resonance absorption at $-60°$. No change in *g* value or line width of the spectrum occurred on cooling. About one-half to one-third of the radical present at 20° appears at $-10°$. In further agreement with these results, the number of spins present at room temperature in the narrow esr signal was always less than half of the oxidized zinc porphyrin molecules. A detailed study is required to resolve several possible explanations of these observations, *e.g.*, temperature-dependent aggregation.

Redox Potentials. No serious attempt was made to reduce the observed potentials to an absolute scale, but some observations were made on the potentials achieved by the oxidants used in methanol. The iodine system (10^{-2} *M*) gave a midpoint potential (always *vs.* sce at ~25°) of ~400 mV. The system is complicated by the fomation of I_3^- (absorption band at 359 nm). Thus the observed potential decreases with increasing I^- concentration. The ferric–ferrous perchlorate system gave stable potentials at 10^{-2} *M*. The midpoint potential was at ~715 mV, with a slope of 65 mV. The decrease of this potential on dilution indicates aggregation. The dichlorodicyanobenzoquinone (DCCB) gave unstable potentials of about 700 mV. The bromine system (3×10^{-2} *M*) had a midpoint potential at about 760 mV with a slope of about 35 mV. The N-bromosuccinimide did not give a reversible potential measurement, but potentials >1 V were easily observable. These potentials are in agreement with the well-characterized metalloporphyrin potentials. Those oxidants lower on the scale than the metalloporphyrins could not oxidize them completely, while those higher did so.

The order of the redox potentials of the metalloporphyrins parallels the qualitative order of stability of these chelates[28] and the electronegativities of the metal ion. If we assume that the binding in the porphyrins and the oxidized porphyrins are qualitatively the same, the difference between the various metalloporphyrins would be proportional to the differences between the ionic charges in the ring. The more negative charge there is in the porphyrin ring, the easier it will be to remove an electron from the ring. This same argument was previously used to explain the ease of photoreduction of free base and protonated porphyrins as compared to metalloporphyrins,[4] and was also used by Felton and Linschitz[6] to explain the order of polarographic reduction potentials of various metalloporphyrins: free base $\ll$ Ni $\leqslant$ Cu < Zn < Mg. Qualitatively similar observations have been made by Clack and Hush.[5] This is just the reverse of the order of the oxidation potentials given in this paper, and of the polarographic oxidation potentials given by Stanienda.[9] Our electrostatic model also explains the great resistance of the stannic and diprotonated porphyrins to oxidation, and their corresponding ease of reduction. Thus a large amount of data on the redox properties of these macrocycles is made reasonable. The charge on the ring of the various metalloporphyrins should be proportional to the electronegativities of the various metal ions. This relation was found in Zerner and Gouterman's[22] calculations. The oxidation potentials of the metalloporphyrins do increase with increasing electronegativity and a plot of the potentials *vs.* electronegativity of the divalent metals on the Pauling scale is quite linear.

An estimate of the extra energy required to remove an electron from the metalloporphyrin with one less unit negative charge can be made. The Coulomb potential of unit charges separated by the diameter of the porphyrin ring, 10 Å, and using the optical dielectric constant, 1.5, is 1 V. The observed differences of ~0.1 V between the various metals suggests about 0.1 of a unit charge increase, algebraically, as one ascends the order

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[28] Reference 1, p 30; J. N. Phillips, *Rev. Pure Appl. Chem.*, 10, 35 (1964).

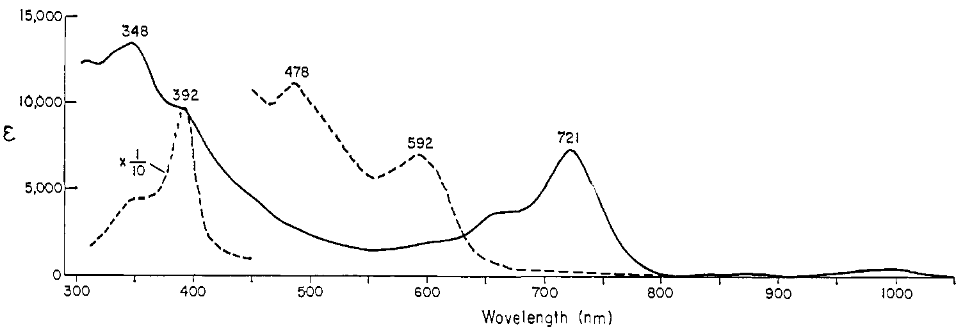

Figure 7. Absorption spectra of ferric octaethylporphyrin hydroxide (— — —) and its (irreversible) oxidation product (———); solvent: methanol-chloroform, 5:1; oxidant: N-bromosuccinimide.

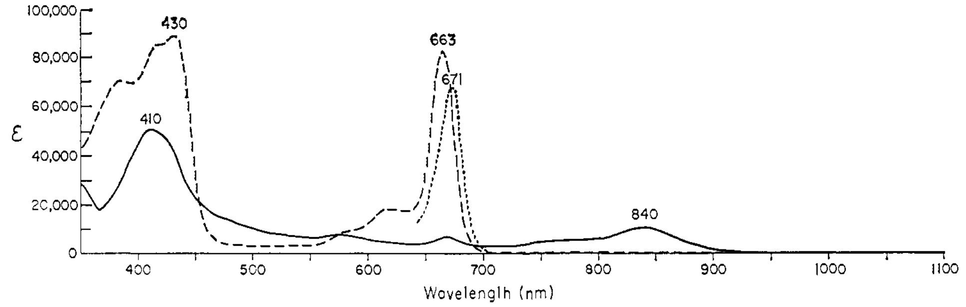

Figure 8. Absorption spectra of chlorophyll a (— — —), its oxidation product (———), and the recovered chlorin (· · ·); solvent: methanol; oxidant: ferric perchlorate.

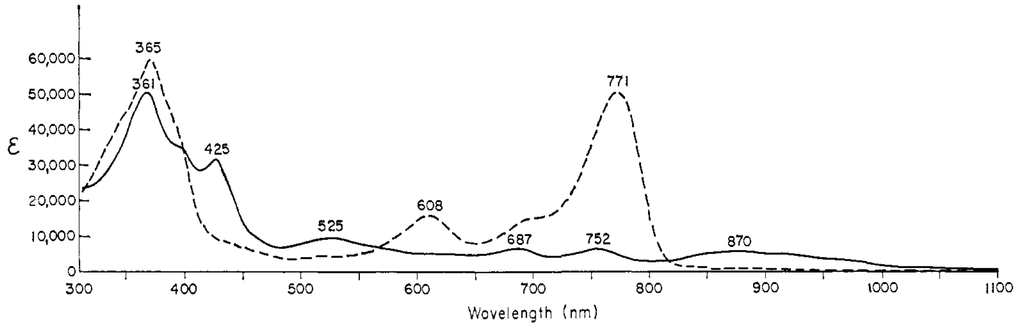

Figure 9. Absorption spectra of bacteriochlorophyll (— — —) and its oxidation product (———); solvent: methanol; oxidant: iodine.

of metals in Table II with a smaller jump between nickel and copper. In fact, the calculations of Zerner and Gouterman[22] give for the net charge in the ring: magnesium, −0.57; zinc, −0.40; nickel, −0.30; copper, −0.28; and protonated dication, +0.85. The agreement with the model is thus quite good.

The polarographic half-wave potentials given by Stanienda[9] for the oxidation of metalloetioporphyrins in butyronitrile are within ±40 mV of the values shown in Table II. He explains the order of the oxidation potentials by the assumption of localized pairs of electrons on nitrogens. These electrons are the one(s) lost on oxidation and are stabilized by hydrogen bonding in the free porphyrin or repelled by the metal ions, essentially as a function of size. This argument fails to correlate the inverse order of the reduction potentials. It also fails to explain the great stability of the stannic porphyrin.

Iron Porphyrin and Chlorophylls. The oxidation of several pigments important in biological systems was studied in a preliminary manner. The ferric octaethylporphyrin hydroxide oxidized at a very high potential (Table II) as expected. Under the conditions used, the reaction was irreversible. The spectrum of the product, Figure 7, resembles that of a phlorin. Such a species may be involved in the catalase and peroxidase reactions about which there is a long-standing controversy concerning the higher oxidation states of the heme.

The oxidation of chlorophyll a in methanol with ferric perchlorate gave a pigment absorbing at 840 and 410 nm (Figure 8). This pigment could be reduced to a chlorin differing from the original chlorophyll. Studies with chlorophyll derivatives and simpler chlorins are required to clarify these reactions.

The oxidation of bacteriochlorophyll was far more reversible and gave stable potentials (Figure 1, Table II). The spectrum of the oxidized product (Figure 9) resembles that obtained by Goedheer.[8] The esr spectrum (Table III) resembles that seen in photosynthetic bacteria and a detailed study will be published elsewhere.

The results presented in this paper may lead to an explanation of the presence of magnesium rather than other metals in photosynthetic pigments. The transition metal chelates may be ruled out because of weak photochemical activity, presumably caused by rapid internal electron transfer. Their lack of fluorescence is consistent with these properties. Zinc would seem to have been the simpler choice, and it does fluoresce. Zinc is both chelated far more firmly (~10^4 times) and enters the ring far more easily. Boucher and Katz[29] have pointed out that zinc chlorophylls aggregate less than the magnesium derivatives. This may have been one cause for the selection of magnesium since chlorophyll *in vivo* is highly aggregated. Our results show that zinc may introduce complications such as two different oxidized species. Moreover, if the aim of the biological system is minimum redox potential combined with maximum stability in a protonic solvent, then magnesium is a good mini-max solution to these requirements.

Acknowledgments. We thank Professor S. Granick for his constant help, and Professor G. Feher at the University of California at San Diego and Dr. R. Shulman at Bell Laboratories, Murray Hill, N. J., for use of their esr apparatus and help with the measurements. We thank Professors R. H. Felton and J. Fajer for showing us their manuscript prior to publication and for several helpful discussions.

This work was supported by grants from the Public Health Service, GM-14827 and GM-04922 and by a NATO fellowship to J. H. Fuhrhop from the Deutscher Akademischer Austauschdienst.

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[29] L. J. Boucher and J. J. Katz, *J. Am. Chem. Soc.*, **89**, 4703 (1967).

Anodic Cyanations of Aromatic Compounds

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Abstract: Electrochemical oxidations of cyanide ion solutions containing aromatic substrates result in three types of cyanation reaction: aromatic substitution of hydrogen; replacement of aromatic methoxyl by nitrile; and introduction of a nitrile group in an α position of tertiary amines. Mechanistic evidence indicates all products are derived from initial oxidation of aromatic substrate and subsequent reaction with cyanide ion. The fate of electrochemically generated cyano radical was investigated by esr spectroscopy.

Previous work[1] on the electrochemical oxidation of cyanide ion in aqueous solution suggested an initial irreversible one-electron process leading to cyanogen which, in basic solution, ultimately yielded cyanate ion. Oxidation products were not detected by chronopotentiometry using current reversal techniques. Although cyano radicals have received considerable study spectroscopically in the vapor phase,[2] relatively few investigations of the chemical fate of cyano radical in the condensed phase have appeared. Cyano radical has been invoked to account for low yields of cyanated products from the photolysis of mercuric cyanides[3] or organomercuric cyanides.[4]

In this paper, we describe results of controlled potential electrochemical oxidations of nonaqueous solutions of cyanide ion in the presence of aromatic substrates to give cyanated products.[5] Electrolysis of silver cyanide in liquid ammonia or pyridine produces cyanogen as a primary product.[6] Recently intervention of cyano radical has been proposed to account for cyanated products obtained from the electrolysis of methanol solutions of sodium[7] or mercuric[8] cyanide in the presence of cyclohexene or aromatic compounds, respectively. The interpretation in the former case has been criticized.[9]

Electroanalytical Studies

To elucidate the primary electrode process or to define intermediate species which might be trapped in subsequent reactions, oxidation of cyanide ion in acetonitrile at a platinum electrode was studied. Chronopotentiometry in CH_3CN revealed a poorly defined, elongated oxidation transition with $E_{1/4} \approx +0.90$ V[10] *vs.* Ag-10^{-2} *M* $AgNO_3$. Data in Table I taken over a 30-fold change in current level clearly show the over-all process to be diffusion controlled. Current reversal produced a small reduction transition at -2.0 V.

Cyclic voltammetric experiments in the potential range -2.5 to $+2.0$ V (sce) revealed an oxidation process at potentials more positive than $+0.5$ V. At lower scan rates ($\approx$0.9 V/sec) discrete but relatively broad peaks were observed. At higher scan rates (up to 263

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[1] D. T. Sawyer and R. J. Day, *J. Electroanal. Chem.*, **5**, 195 (1963).

[2] D. E. Paul and F. W. Dalby, *J. Chem. Phys.*, 37, 592 (1962); D. Schofield, W. Tsang, and S. H. Bauer, *ibid.*, 42, 2132 (1965); M. Jeunehomme, *ibid.*, 42, 4086 (1965); S. H. Bauer and W. S. Watt, *ibid.*, **44**, 1327 (1966); K. M. Evenson and H. P. Broida, *ibid.*, **44**, 1637 (1966); C. A. Gay, D. H. Shaw, and H. O. Pritchard, *J. Phys. Chem.*, **69**, 1504 (1965); J. A. Knight, R. A. Stokes, and D. Bowen, *ibid.*, **69**, 678 (1965); N. Basco and R. G. W. Norrish, *Proc. Roy. Soc.* (London), **A283**, 291 (1965). Esr detection of cyano radical in a solid argon matrix was also reported: E. L. Cochran, F. J. Adrian, and V. A. Bowers, *J. Chem. Phys.*, **36**, 1938 (1962).

[3] K. Yoshida and S. Tsutsumi, *Tetrahedron Letters*, 2417 (1965); *J. Org. Chem.*, **31**, 3835 (1966).

[4] K. Yoshida and S. Tsutsumi, *Tetrahedron Letters*, 281 (1966).

[5] Part of this work was presented at the Spring Meeting, Electrochemical Society, Dallas, Texas, May 1967: S. Andreades and E. W. Zahnow, Extended Abstracts, I-4, p 15.

[6] H. Schmidt and H. Meinert, *Z. Anorg. Allgem. Chem.*, **295**, 156 (1958); A. von Krusenstjern and J. Meier, *Metalloberflaeche*, **18**, 330 (1964).

[7] K. Koyama, T. Susuki, and S. Tsutsumi, *Tetrahedron Letters*, 627 (1965); *Tetrahedron*, **23**, 2675 (1966).

[8] K. Yoshida and S. Tsutsumi, *Tetrahedron Letters*, 2501 (1966).

[9] V. D. Parker and B. E. Burgert, *ibid.*, 4065 (1965); 2415 (1968).

[10] The potential of the Ag-10^{-2} *M* $AgNO_3$ electrode in CH_3CN *vs.* aqueous sce has been reported as $+0.30$ V: R. C. Larson, R. T. Iwamoto, and R. N. Adams, *Anal. Chim. Acta*, **25**, 371 (1961).