C. Attempted Condensation of Glycolaldehyde with 1-*O*-α-D-Glucopyranosyl-L-glycerol.—A mixture of 1-*O*-α-D-glucopyranosyl-L-glycerol (21 mg, 0.082 mmol) and glycolaldehyde (32 mg, 0.53 mmol) in methanol (1 ml) was treated with 1 *N* methanolic hydrogen chloride (0.38 ml) for 18 hr at 20°. The reaction mixture was neutralized with silver carbonate and filtered, and the solution was concentrated. The unreacted glucosylglycerol was the only component visible by paper chromatography in solvents A and E. Acetals **4** and **5** could not be detected.

Hydrolysis of the Dextran Polyalcohol.—The dextran polyalcohol was hydrolyzed with 0.1 *N* hydrochloric acid at 25° for 18 hr, and the reaction mixture was neutralized and treated with sodium borohydride. The components of the deionized hydrolysate were separated by paper chromatography. The same components (i–vi) were identified, but in addition there were small amounts of several components which appeared to be condensation products of these components with glycolaldehyde or glyceraldehyde. These were not investigated further.

Synthesis of 1-*O*-α-D-Glucopyranosyl-L-glycerol.—A solution of isomaltitol (0.245 g) in water (1 ml) was diluted with acetic acid (75 ml) and treated with lead tetraacetate (0.350 g, 1.1 molecular proportions). The reaction mixture was shaken vigorously until the lead tetraacetate had dissolved and, after 2.5 hr at room temperature, oxalic acid (0.368 g) in acetic acid (10 ml) was added. The mixture was filtered and the solution was concentrated. The residue was dissolved in water and deionized with Amberlite IR-120 (H^+) and Duolite A-4 (OH^-) resins. Sodium borohydride (0.20 g) was added, and after 15 hr the solution was neutralized with acetic acid and the sodium ions were removed with Amberlite IR-120 (H^+). The solution was concentrated, and the residue was treated with methanol to remove boric acid.

Preparative paper chromatography (solvent G) of the syrupy product (0.204 g) afforded pure 1-*O*-α-D-glucopyranosyl-L-glycerol (0.070 g) in addition to isomaltitol (0.054 g), 1-*O*-α-D-glucopyranosyl-L-erythritol (0.011 g), and hydroxyethyl α-D-glucopyranoside (0.030 g). The 1-*O*-α-D-glucopyranosyl-L-glycerol had $[\alpha]^{29}D$ +123.9° (*c* 1.2, water) and on heating with pyridine and *p*-nitrobenzoyl chloride at 95° for 3.5 hr it gave a hexa-*p*-nitrobenzoate which was recrystallized from acetone–ethanol (1:1): mp 121–125°, solidifying and remelting at 222–223°; $[\alpha]^{24}D$ +57.4° (*c* 1.0, acetone).

Anal. Calcd for $C_{51}H_{36}N_6O_{26}$: C, 53.3; H, 3.2; N, 7.3. Found: C, 53.2; H, 3.2; N, 7.1.

Registry No.—Isomaltose β-acta-*p*-nitrobenzoate, 16780-53-3; 1-*O*-α-D-glucopyranosyl-L-glycerol hexa-*p*-nitrobenzoate, 16808-40-5.

Acknowledgments.—This work was supported by funds from the U. S. Public Health Service, Department of Health, Education and Welfare, Grant No. GM 11737-01. M. J. St. Cyr was the recipient of a fellowship under Pathology Training Grant No. 5T1, GM 628-04, U. S. Public Health Service. The authors thank Dr. E. J. Hehre for the polysaccharide.

Deoxophylloerythroetioporphyrin[1a]

EARL W. BAKER,[1b,c] ALSOPH H. CORWIN,[1c] ERNST KLESPER,[1c] AND P. E. WEI[1c]

Mellon Institute, Carnegie-Mellon University, Pittsburgh, Pennsylvania 15213, and the Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

Received September 14, 1967

A method of preparation of deoxophylloerythroetioporphyrin using the chlorophyll derivative, pheophytin, as the starting material has been worked out. In the procedure pheophytin is first converted into pyropheophorbide which is further degraded to deoxophylloerythrin in a single composite reaction based on the Wolff–Kishner reduction. Deoxophylloerythrin is then decarboxylated to yield deoxophylloerythroetioporphyrin by a seven-step reaction which includes Curtius rearrangement, Hofmann degradation, and catalytic hydrogenation.

The natural occurrence of deoxophylloerythroetioporphyrin (DPEP) was suspected by A. Treibs when he extracted from a Swiss marl a porphyrin with a visible spectrum identical with that of deoxophylloerythrin (for structures see Table I) and chemical properties indicating the absence of carboxyl groups.[2] The central position of DPEP in the geochemistry of the fossil porphyrins[3] required that the suggested structure be confirmed by synthesis. Using the usual synthetic approach of the Fischer school based on the appropriate pyrromethenes, an authentic sample of DPEP was prepared. However, the yields were dishearteningly low; for example, 12 mg of DPEP was obtained from 30 g of pyrromethenes.[4] A later attempt by other workers to repeat the synthesis produced only fractional milligrams of the desired porphyrin and they reported that the major product was etioporphyrin.[5] The comparative ease with which quantities of the chlorophyll derivative, pheophytin, can be obtained from natural sources suggested that a different approach might be more fruitful. Since it already contains the required carbon skeleton, the choice of pheophytin as the starting point would avoid much of the tedium of the pyrromethene synthesis. Furthermore, now that the structure of chlorophyll has been confirmed,[6] it is sound to use it as a starting point for the synthesis of compounds of related structures.

Thus, a logical starting point for the synthesis of DPEP was pheophytin a + b (see Table II). Pheophytin is produced by extraction from chlorophyll-rich plants and may be obtained commercially. It is known to be readily converted into pyropheophorbide a + b by refluxing in concentrated HCl, and so could be made available in quantity without undue labor. A glance

(1) (a) Porphyrin Studies. XXXVI. Paper XXXV: C. B. Storm, A. H. Corwin, R. R. Arellano, M. Martz, R. Weintraub, *J. Amer. Chem. Soc.*, **88**, 2525 (1966). This work supported in part by the Petroleum Research Fund administered by the American Chemical Society and in part by Public Health Service Research Grant No. FR 55801-5 from the General Research Support Branch. (b) Mellon Institute. (c) Johns Hopkins University.

(2) A. Treibs, *Ann.*, **509**, 103 (1934).

(3) (a) For the orginal proposal of the organic geochemistry of the porphyrins, see A. Treibs, *Angew. Chem.*, **49**, 682 (1936); (b) for a recent discussion, see E. W. Baker, in "Organic Geochemistry: Methods and Results," G. Eglinton and M. Murphy, Ed., Springer-Verlag, New York, N. Y., 1968.

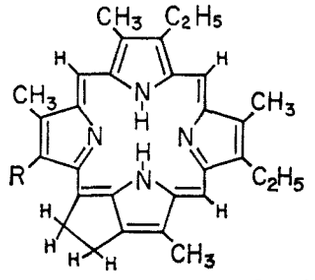
(4) H. Fischer and H. J. Hoffmann, *Ann.*, **517**, 274 (1935).

(5) J. M. Sugihara and L. R. McGee, *J. Org. Chem.*, **22**, 795 (1957). These workers suggest etioporphyrin I as the major product from the reaction mixture. However, the proximate 2-carbon side chains (3′-ethyl and 3-bromovinyl) on the pyrromethene component which forms the III and IV rings of the porphyrin seem to contradict this and etioporphyrin III would be the product if the isocyclic ring did not close.

(6) (a) R. B. Woodward, *Pure Appl. Chem.*, **2**, 383 (1961); (b) R. B. Woodward, *et al.*, *J. Amer. Chem. Soc.*, **82**, 3800 (1960); (c) for a complete discussion of all details of this synthesis and prior work, see W. Lwowski in "The Chlorophylls," L. P. Vernon and G. R. Seely, Ed., Academic Press, New York, N. Y., 1966, p 119.

TABLE I

STRUCTURE AND NAMES OF PORPHYRINS



Compound name: trivial (systematic)	Compd no.	R	Reactants and conditions
Deoxophylloerythrin (1,3,5,8-tetramethyl-2,4-diethyl-6,γ-ethanoporphine-7-propionic acid)	V	CH_2CH_2COOH	CH_3OH, HCl
Deoxophylloerythrin methyl ester (1,3,5,8-tetramethyl-2,4-diethyl-6,γ-ethanoporphine-7-propionic acid methyl ester)	VI	$CH_2CH_2COOCH_3$	$NH_2NH_2 \cdot H_2O$
Deoxophylloerythrin hydrazide (1,3,5,8-tetramethyl-2,4-diethyl-6,γ-ethanoporphine-7-propionic acid methyl ester)	VII	$CH_2CH_2CONHNH_2$	HNO_2, MeOH
Deoxophylloerythrin ethyl-ω-methylurethan [1,3,5,8-tetramethyl-2,4-diethyl-6,γ-ethano-7-(ethyl-ω-methylurethan)porphine]	VIII	$CH_2CH_2NHCOOCH_3$	10% HCl, 130°
Deoxophylloerythrin ethyl-ω-amino hydrochloride [1,3,5,8-tetramethyl-2,4-diethyl-6,γ-ethano-7-(ethyl-ω-amino hydrochloride)porphine]	IX	$CH_2CH_2NH_3^+Cl^-$	OH^-, $(CH_3)_2SO_4$
Deoxophylloerythrin ethyl-ω-dimethylamino dimethyl sulfate [1,3,5,8-tetramethyl-2,4-diethyl-6,γ-ethano-7-(ethyl-ω-dimethylamino dimethyl sulfate)-porphine]	X	$CH_2CH_2N^+(CH_3)_3SO_4CH_3^-$	KOH, heat
Protodeoxophylloerythroetioporphyrin (1,3,5,8-tetramethyl-2,4-diethyl-7-vinyl-6,γ-ethanoporphine)	XI	$CH{=}CH_2$	H_2–Pt, THF
Deoxophylloerythroetioporphyrin (1,3,5,8-tetramethyl-2,4,7-triethyl-6,γ-ethanoporphine)	XII	CH_2CH_3	

at the formulas shows that the route from pyropheophorbide to DPEP crosses two major hurdles. The oxidation level of a number of the substituents (reduction of carbonyl and vinyl) as well as that of the aromatic system (oxidation of chlorin to porphyrin) must be changed and decarboxylation of a propionic acid side chain must be performed. Decarboxylation of unactivated carboxyl groups is difficult and in this case is more so owing to the ponderance of the molecule. Methods of decarboxylation of the propionic acid group were considered and the Curtius and Hofmann degradative method was the obvious choice because of its demonstrated utility on porphyrin carboxylic acids. All reactions in this sequence proceed under relatively mild conditions such that the integrity of the porphyrin moiety is known to be preserved.[7] The reaction sequence is somewhat lengthy (eight steps) and yields are considerably less than quantitative. These considerations dictated that deoxophylloerythrin would have to be made available in sizable quantities. To this end then, first attention was devoted to streamlining and simplifying the standard methods of reducing the functional groups of pyropheophorbide and oxidizing it to a porphyrin.

It was known that the Wolff–Kishner reaction run under mild conditions would reduce both the vinyl and carbonyl functions of pyropheophorbide a or b to give, along with several other products, deoxomesopyropheophorbide (III).[8] Under more severe Wolff–Kishner conditions, some deoxophylloerythrin and etioporphyrin III were formed.[9] Reduction of the carbonyl functions and the aromatization are, of course, not unexpected but clean reduction of the vinyl group does not occur under Wolff–Kishner conditions in a sealed tube. The fact that the effective reductant is not hydrazine but its oxidation product, diimide, explains this observation.[10]

Thus, an improved procedure, based on the above considerations and incorporating the Huang-Minlon modification of the Wolff–Kishner reduction, was formulated. Pyropheophorbide a + b is converted into deoxophylloerythrin in one composite reaction without isolation of the intermediates. Three distinct reactions take place sequentially: reduction of the vinyl group, reduction of the carbonyl functions, and dehydrogenation of ring IV. The early stages of the reaction are run in the presence of air to obtain reduction of the vinyl group. If oxygen is carefully excluded from the reaction mixture, a sizable yield of what appears to be the 2-vinyl analog of deoxophylloerythrin is obtained; however, some reduction of the vinyl group still occurs even in the absence of oxygen. In a later stage of the reaction, base is added and the temperature raised to 150° to decompose the hydrazone (IV). Finally, the temperature is raised to 190–200° and the reaction mixture changes from dull green to reddish brown indicating conversion into the porphyrin, which after work-up is obtained in about 65% yield. A small yield of chlorin is also obtained which spectral evidence indicates is deoxomesopyropheophorbide (III).[8]

(7) For example, see (a) mesoporphyrin IX to etioporphyrin III, E. W. Baker, M. Ruccia, and A. H. Corwin, *Anal. Biochem.*, **8**, 512 (1964), and H. Fischer, E. Haarer, and F. Stadler, *Z. Physiol. Chem.*, **241**, 201 (1936); (b) koproporphyrin I to 1,3,5,7-tetramethyl-2,4,6,8-tetravinylporphine, H. Fischer, *et al.*, *ibid.*; (c) pyrroporphyrin XV to pyrroetioporphyrin, H. Fischer and E. Haarer, *ibid.*, **229**, 55 (1934).

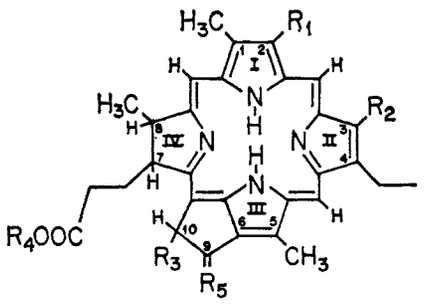
(8) (a) H. Fischer and H. Gibian, *Ann.*, **552**, 153 (1942); (b) *ibid.*, **548**, 183 (1941).

(9) H. Fischer, E. Lakatos, and J. Schnell, *ibid.*, **509**, 212 (1934).

(10) (a) E. J. Corey, W. L. Mock, and D. J. Pasto, *Tetrahedron Lett.*, No 11, 347 (1961); (b) E. J. Corey, D. J. Pasto, and W. L. Mock, *J. Amer. Chem. Soc.*, **83**, 2957 (1961).

TABLE II

STRUCTURE OF PHORBIDES



Name	Compd no.	R_1	R_2 a	R_2 b	R_3	R_4	R_5
Pheophytin	I	$CH{=}CH_2$	CH_3	CHO	$COOCH_3$	$C_{20}H_{39}$	O
Pyropheophorbide	II	$CH{=}CH_2$	CH_3	CHO	H	H	O
Deoxomesopyropheophorbide	III	CH_2CH_3	CH_3	CHO	H	H	H_2
Pyropheophorbide hydrazone	IV	$CH{=}CH_2$	CH_3	$CH{=}NNH_2$	H	H	NNH_2

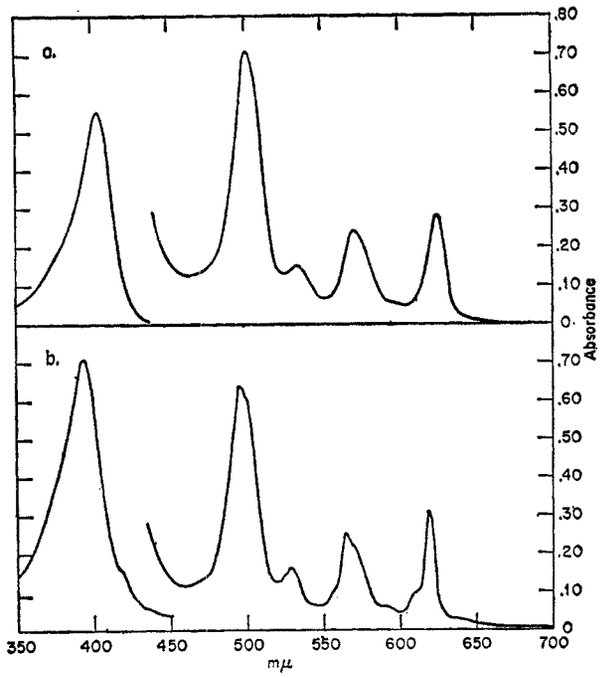


Figure 1.—(a) Electronic spectrum of protodeoxophylloerythroetioporphyrin; (b) electronic spectrum of deoxophylloerythroetioporphyrin.

Deoxophylloerythrin was then decarboxylated to yield DPEP by the series of reactions shown schematically in Table I. In all reactions, the conditions used were essentially those reported for the conversion of mesoporphyrin IX into etioporphyrin III,[7a] except for the formation of deoxophylloerythrin hydrazide. Conditions under which no mesoporphyrin dimethyl ester was reduced, produced chlorin as the major product when deoxophylloerythrin methyl ester was treated with hydrazine hydrate. To obtain deoxophylloerythrin hydrazide, less severe conditions were employed; and the unconverted material was recovered and recycled. The reaction conditions reported (see Experimental Section) represent a compromise between unproductive recycling and loss of material by reduction. Except for the quaternary salt (X), all intermediates in the decarboxylation sequence were crystallized and characterized. Not surprisingly, the quaternary salt undergoes elimination so readily that pure crystalline material was not obtained. This ready elimination is in no way detrimental to the synthesis; and, as the procedures evolved, it was found that higher yields were obtained by treating the total precipitate with base and recovering the vinyl compound (XI). The vinyl compound (proto DPEP) was catalytically hydrogenated to DPEP. In the product, a small absorption in the chlorin region (645 mμ) was observed. Mesoporphyrin does not reduce to chlorin under similar conditions even on extended hydrogenation. It is clear from these results that the isocyclic ring causes the molecule to be much more readily reduced.

Preparation of Metallo Chelates.—Vanadyl sulfate and acetic acid are effective in introducing vanadyl into porphyrins of the etio series; however, the insoluble vanadyl porphyrin coats the vanadyl sulfate particles and prevents the reaction from going to completion.[11] Addition of a cosolvent such as pyridine or dimethylformamide provides a homogeneous reaction mixture and overcomes this problem. Dimethylformamide is the cosolvent of choice when higher temperatures are required. Interestingly, the effect of the isocyclic ring was again noticed in the preparation of the vanadyl complexes. Considerably higher temperatures than those needed for the preparation of vanadyl mesoporphyrin failed to produce vanadyl deoxophylloerythrin. Addition of a small amount of trichloroacetic acid causes the reaction to proceed at a temperature of *ca.* 130°.

The formation of nickel chelates did not seem to be subject to such effects, and they were prepared in the standard way with nickel acetate in glacial acetic acid.

Electronic Spectra.—The visible spectra of all the derivatives of deoxophylloerythrin were identical (compounds V–X). Since only alterations to the side chain 2 or more carbons from the ring were being performed, this is expected. Only when the quaternary salt (X) decomposed to give a vinyl group in conjugation with the ring, did a noticeable change occur (compare parts a and b of Figure 1). The spectrum of the vinyl compound was shifted 6 mμ to longer wavelength compared to deoxophylloerythrin and much of the fine

(11) J. G. Erdman, V. G. Ramsey, N. W. Kalenda, and W. E. Hanson, *J. Amer. Chem. Soc.*, **78**, 5844 (1956).

structure which can be easily seen in the other spectra is missing (note especially the near absence of the Ia peak at 588 mμ). These spectral differences are analogous to those in protoporphyrin and etioporphyrin where much more fine structure can be seen in the etio spectrum and a shift of *ca.* 6 mμ per conjugated vinyl group has been noted.[12]

Steric Factors.—In a number of other cases where the hydrazides of porphyrin carboxylic acids were prepared by Fischer and coworkers under much more severe conditions (up to 30-hr reaction time) than employed here, no examples of reduction to chlorins are reported.[13] In none of the cases, however, did the porphyrin carboxylic acids contain an isocyclic ring.

An explanation for the ease of reduction of certain specifically substituted porphyrins has been advanced by Woodward.[6] The lower periphery of porphyrins (as the formula is usually drawn) derived from chlorophyll (such as DPEP) is so heavily laden with substituents that there is not room for all of them to lie in the plane of the ring. Hence, there is considerable distortion of bond angles and lengths. Removal of hydrogen atoms from the 7 and 8 positions of a 6,γ,7-substituted chlorin (for example, pyropheophorbide) transforms carbons 7 and 8 from tetrahedral to trigonal hybridization.

In the trigonal hybridization, substituents are forced into the plane of the ring with resultant distortion of bond angles and lengths. Conversely, there is a strong steric factor which favors the conversion of trigonal carbons, 7 and 8, into tetrahedral ones. Said another way, this means that such porphyrins (*i.e.*, DPEP) are rather easily reduced to chlorins. If the steric factor is absent as in the case of etioporphyrins, the reduction to chlorins occurs only under severe conditions.

Steric arguments similar to those advanced above probably also obtain for the reduction of the 9-carbonyl group to CH_2. The planar oxygen substituent is replaced by two *nonplanar* protons thus alleviating the peripheral crowding. At the same time, the carbonyl carbon is converted from trigonal (120°) into tetrahedral (109°) hybridization, with the concomitant approach to the unstrained 108° interior angle of a five-membered ring.

Naming of Compounds.—It has been convenient to use trivial names in accord with the conventions of Fischer for the new compounds rather than systematic names as substituted porphines. For example, compound (XI) has been called protodeoxophylloerthroetioporphyrin (proto DPEP) rather than 1,3,5,8-tetramethyl-2,4-diethyl-7-vinyl-6,γ-ethanoporphine. The prefix proto in this case showing the same relationship as protoetioporphyrin does to etioporphyrin.[14] The earlier compounds in the series were designated as derivatives of deoxophylloerythrin. Both systematic and trivial names are given in Table I including those for new compounds VII–XI.

(12) J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier Publishing Co., New York, N. Y., 1964, p 77.

(13) See examples in ref 8 and also H. Fischer and E. Thurner, *Z. Physiol. Chem.*, **204**, 79 (1932).

(14) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. II, part I, Akademie Verlag, Leipzig, 1937, p 218.

Experimental Section[15]

Pyropheophorbide a + b.—Pheophytin a + b[16] (I) (4.0 g) was stirred with acetone (250 ml) in a Waring Blendor for 5 min. The solution was decanted into a 4-l. beaker and the solvent was evaporated on a steam bath under nitrogen until a gummy residue remained. (Allow some acetone to remain to promote solubility in the ether.) Peroxide-free ether (800 ml) was added with stirring to dissolve the pheophytin. Concentrated (36%) HCl (2 l.) was added slowly and the solution was heated on steam bath at boiling temperature for 1 hr. Cold water (800 ml was added and the solution was transferred to a 6-l. separatory funnel. After two extractions with ether (1 l.) to remove the phytol, one-half of the acid solution was placed in a 6-l. separatory funnel, and cold water (2.5 l.) was added. Extraction with successive 1-l. portions of ether (total 6 to 7 l.) was continued until the aqueous layer was pale green. The aqueous layer was then discarded and the second portion was treated in a like manner. The ether extracts were combined and evaporated giving bright green glassy flakes,[17] yield 1.85–1.95 g (65–70%).

Deoxophylloerythrin (V).—Pyropheophorbide a + b (2.0 g) was added to triethylene glycol (300 ml) and 99% hydrazine hydrate (15 ml) in a 500-ml, round-bottom flask fitted with a heater and stirrer. The mixture was heated at 100° for 2 hr in contact with air with constant stirring. NaOH (15 g) was added, the solution was blanketed with nitrogen, and the temperature was raised *carefully* to 150–160° when loss of nitrogen, from hydrazone occurred with frothing of the solution. When the gas evolution was complete, the temperature was raised to 190–210° and maintained for 1 hr. During this time, the reaction mixture changed from a dull green to a reddish brown indicating the formation of porphyrin. The reaction mixture was cooled and poured into 5% HCl (1 l.). After extracting twice with 750-ml portions of ether to remove unconverted chlorin, anhydrous sodium acetate was added to the aqueous layer to pH 5. The precipitate, coagulated by warming, was cooled, filtered, washed with distilled water, and dried at 60° to obtain 1.2–1.35 g (60–68%) of vermillion powder: low resolution mass spectra, 70 eV, *m/e* (%) 520 (100) (P), 505 (6) ($P - CH_3^+$), 416 (17) ($P - CH_2COOH^+$). The molecular ion at 492 may indicate that devinylation rather than reduction occurs to a small degree (3%) to give 2-desethyl deoxophylloerythrin. The molecular ion at 494 is not easily explainable but could indicate rupture and loss of the carbocyclic ring. The electronic spectrum was identical with that of the methyl ester (VI).

Deoxophylloerythrin Methyl Ester (VI).—To deoxophylloerythrin (V) (2.0 g) in a 500-ml flask was added absolute MeOH (200 ml), and *dry* nitrogen was passed through for a short time. Gaseous HCl was then added at a rapid rate until the solution was saturated and initial generation of heat was finished. After 20 min, the flow of HCl was reduced and the reaction flask was cooled with an ice bath; however, cooling is probably not necessary since, in some cases, higher yields were obtained without cooling. Slow HCl flow was continued for 1 hr. Then the methanol–HCl solution was poured into a 6-l. separatory funnel containing 2 l. of ice water and ether (1 l.) added. The solution was neutralized to pH 5 with dilute aqueous ammonia (1:1)

(15) Elemental analyses were performed by Mr. J. Walter at the Chemical Laboratories of The Johns Hopkins University. Mass spectra and exact molecular weights were determined on an AEI MS9 double-focusing mass spectrometer by Mr. R. E. Rhodes of Research Services at the Mellon Institute. Electronic spectra were recorded on a Beckman DK-2 spectrophotometer.

(16) Pheophytin a + b is obtainable commercially from a number of suppliers. Alfalfa meal is generally the source of domestic supplies whereas the European source is more commonly stinging nettle leaves. In our hands the latter material was easier to process, being less prone to form persistent emulsions in the phytol separation step and giving pyropheophorbide without gummy contaminants. However, experience with a wide variety of starting materials, some of questionable purity, showed that all were workable and apparently all produce equivalent purity material at the deoxophylloerythrin methyl ester stage. For details on methods of extraction of chlorophyll from plant sources, see R. Willstätter and A. Stoll, "Investigations on Chlorophyll, translated by F. Schertz and A. Merz, Science Printing Press, Lancaster, Pa., 1928, p 48.

(17) The visible spectrum showed peaks at 663, 655, 604, 560, 530, and 501 mμ indicative of a mixture of pyropheophorbide a + b. The procedure was checked by treatment of the a component obtained by acid fractionation (ref 14, part II, p 56). The product in that case showed absorption peaks at 663, 605, 560, 533, and 501 mμ identical with those of authentic pyropheophorbide a [A. Stoll and E. Wiederman, *Helv. Chim. Acta*, **17**, 837 (1934)] and did not give a phase test.

while keeping the temperature at 0–5° by the addition of cracked ice. After separation and reextraction of the water layer with successive 1-l. portions of ether, the unesterified material which precipitated at the interface was recovered by filtration of the water layer. The ether extracts were combined and passed through a 35 × 150 mm column of Alcoa Grade F 80–200 mesh alumina. The ether was reduced to low volume on a steam bath and the product was recovered by filtration. A yield of raw product of 1.3–1.5 g (65–75%) was obtained. The product was recrystallized from 1:10 chloroform–methanol to give blue-black prisms: mp 262° (lit.[18] 264°); spectrum in benzene, λ_{max} 619 mμ (ε 7.1 × 10³), 562 (6.8 × 10³), 527 (3.8 × 10³), 495 (17 × 10³), 393 (220 × 10³) [lit.[19] 615 (6.5 × 10³) 564 (6.3 × 10³), 530 (3.56 × 10³), 496 (16.67 × 10³)].

Vanadyl Deoxophylloerythrin Methyl Ester.—Deoxophylloerythrin methyl ester (0.2 g) and vanadyl sulfate (0.2 g) were dissolved in DMF (10 ml) in a three-necked flask equipped with a nitrogen inlet tube, a stirrer, and condenser. Trichloroacetic acid (1.0 g) dissolved in glacial acetic acid (10 ml) was added and the solution was heated to 120–130° for 1 hr. Warm water (7 ml) was added dropwise, and, after cooling, the crude product was recovered by filtration to yield 0.2 g.

The crude material was dissolved in benzene and chromatographed on Davison No. 62 silica gel. Unreacted deoxophylloerythrin methyl ester was eluted with 50:50 benzene–cyclohexane and the vanadyl chelate was eluted with benzene. The elutant was reduced to low volume and five parts of methanol was added to induce crystallization: in benzene, λ_{max} 568, 528, 405 mμ; rel OD 1.0, 0.77, *ca.* 15.

Anal. $C_{34}H_{36}N_4O_3V$: C, 68.1; H, 6.05. Found: C, 68.3; H, 6.03.

Deoxophylloerythrin Hydrazide (VII).—Deoxophylloerythrin methyl ester (2.0 g) was treated with 98% hydrazine hydrate (8 ml) in absolute MeOH (50 ml) for 7.5 hr at 125°, in a glass-lined bomb tube fitted to a low speed shaker. After cooling, the product was separated by filtration and washed with a small quantity of cold MeOH. The deep green filtrate was diluted with water and filtered to recover the reduced by-product. The yield of hydrazide was 1.35 g (68%). The analytical sample was recrystallized from chloroform–methanol. The spectrum is identical with that of the methyl ester.

Anal. Calcd for $C_{33}H_{38}ON_6$ (534.68): C, 74.1; H, 7.16. Found: C, 73.9; H, 7.32.

The yield of reduced by-product obtained depended on the conditions of the reaction, with longer reaction times leading to greater amounts. Spectrally, the material resembles deoxomesopyropheophorbide (III): spectrum in benzene, λ 643, 584, 528, 492, 387 mμ; rel OD, 1.0, 0.12, weak, 0.38, 4.7 (lit.[8b] 647, 584, 524, 493 mμ); order of intensity, I, IV, II, III.

Deoxophylloerythrin Ethyl-ω-methylurethan (VIII).—Deoxophylloerythrin hydrazide (1.0 g) was dissolved in ice-cold 5% HCl (100 ml) and cold 10% sodium nitrite solution added dropwise until potassium iodide paper turned blue. After standing 1.5 hr in the refrigerator, the reaction mixture was dissolved in ethylene dichloride (1.5 l.), and the aqueous layer was separated and reextracted with ethylene dichloride (0.5 l.). The combined ethylene dichloride extracts were washed with 5% NaOH solution (0.5 l.) and then with distilled water (1.0 l.). The ethylene chloride solution was reduced in volume to *ca.* 500 ml on a rotary evaporator and heated on a steam bath to boiling, MeOH was added (200 ml), and the volume further reduced to *ca.* 200 ml. The remainder of the ethylene dichloride was displaced by the addition of methanol (100 ml) and further heating. The methanol solution was chilled overnight in a refrigerator and the product was recovered by filtration to yield 0.55 g (53%).

The visible spectrum was identical with that of the methyl ester.

Anal. Calcd for $C_{34}H_{39}O_2N_5$ (549.69): C, 74.3; H, 7.15. Found: C, 74.3; H, 7.26.

Deoxophylloerythrin Ethyl-ω-amino Hydrochloride (IX).—Deoxophylloerythrin ethyl-ω-methylurethan (1.0 g) was heated with 10% HCl (150 ml) in a glass-lined bomb with shaking for 10 hr. After cooling (16 hr) the crystallized hydrochloride was recovered by filtration and washed with a little 10% HCl. The yield was small and the compound was very hygroscopic. The spectrum in 10% HCl was identical with that of the dication of the methyl ester: λ_{max} 596, 552, and 404 mμ.

Anal. Calcd for $C_{32}H_{40}N_5Cl_3$(600.04): C, 64.05; H, 6.55. Found: C, 62.3; H, 6.67.

Protodeoxophylloerythroetioporphyrin (XI).—Deoxophylloerythrin ethyl-ω-methylurethan (1.0 g) was treated with 10% HCl (150 ml) in a glass-lined bomb with shaking at 130° for 7.5 hr. The amine was precipitated by the addition of 10% sodium acetate, and recovered by centrifugation. While still wet, it was treated with 10% sodium hydroxide (100 ml) and dimethyl sulfate (10 ml) and shaken vigorously for 2 hr at 30°. The precipitated quaternary amine sulfate (X) was recovered by filtration and extracted from the filter with hot methanol. The methanol was reduced in volume to 100 ml and KOH (10.0 g) added. The solution was refluxed for 3.0 hr and cooled. The product was collected by filtration and washed with water, yield 240 mg. The visible spectrum in benzene is shown in Figure 1a: λ_{max} 624 mμ (ε 6.2 × 10³), 571 (5.3 × 10³), 533 (3.3 × 10³), 502 (15.5 × 10³), 404 (183 × 10³).

Deoxophylloerythroetioporphyrin (XII).—Protodeoxophylloerythroetioporphyrin (XI) (200 mg) was dissolved in tetrahydrofuran (200 ml) and PtO_2 catalyst (0.10 g) was added. The reduction was carried out for 20 hr at 1 atm of hydrogen pressure. The solution was filtered to remove the catalyst and the solvent was evaporated to give an essentially quantitative yield of crude product. The visible spectrum showed in addition to the deoxophylloerythrin type spectrum (Figure 1b) a small peak in the 645-mμ region.

The crude product (120 mg) was chromatographed over 30 g of Davison No. 62 silica gel, with 1:1 benzene–cyclohexane as the eluant. [The forerun contained the green (645 mμ) material.] The solvent was removed under vacuum to yield 100 mg of product with the visible spectrum shown in Figure 1b. A portion was recrystallized from benzene–methanol: low resolution mass spectrum, 70 eV, *m/e* (%) 478 (6) (P + 2⁺), 477 (33) (P + 1⁺), 476 (100) (P⁺), 461 (27) (P − CH_3^+) 477 (3) (P + 1 − $2CH_3^+$), 446 (5) (P − $2CH_3^+$), 431 (6), 429 (6); low resolution mass spectrum, 12 eV, *m/e* (%) 478 (7), 477 (31), 476 (100). No other peaks were observed above the noise level between *m/e* 478 and 239. (Calcd for parent peak $C_{32}H_{36}N_4$: 476.291. Found by high resolution mass spectrometry: 476.284.) The electronic spectrum in benzene had absorptions at λ_{max} 618 mμ (ε 7.3 × 10³), 563 (6.6 × 10³), 528 (3.9 × 10³), and 495 (19 × 10³).

Vanadyl Deoxophylloerythroetioporphyrin.—Crude deoxophylloerythroetioporphyrin (20 mg) was dissolved in DMF (5 ml) and treated with vanadyl sulfate (50 mg), trichloroacetic acid (0.5 g), and glacial acetic acid (5 ml). The reaction mixture was blanketed with nitrogen and heated to 125–135° for 1 hr. The mixture was cooled, diluted with water, and filtered. The crude product was taken up in a minimum of benzene and chromatographed over silica gel. A forerun of a small amount of uncomplexed porphyrin was eluted with 50:50 benzene–cyclohexane and the vanadyl complex was recovered by elution with benzene. The eluant was reduced to low volume and five volumes of methanol was added to induce crystallization. The product was recovered as purplish black pyramids:[20] yield 10 mg; in benzene λ_{max} 570, 529, 405 mμ; rel OD 1.0, 0.77 (Calcd for $C_{32}H_{34}N_4VO$: 541.217. Found by high resolution mass spectrometry: 541.210.).

Nickel Deoxophylloerythroetioporphyrin.—Crude deoxophylloerythroetioporphyrin (50 mg) was treated with nickel acetate (50 mg) in glacial acetic acid (10 ml) at reflux temperature for 0.5 hr. The volume of acetic acid was reduced to *ca.* 4 ml with a stream of nitrogen, and the reaction mixture was allowed to cool. The nickel chelate was recovered by filtration as very small red crystals: yield 8 mg; spectrum in benzene, λ_{max} 550, 521, 392 mμ; rel OD, 1.0, 0.51 (Calcd for $C_{32}H_{34}N_4Ni$: 532.214. Found by high resolution mass spectrometry: 532.214).

Registry No.—VII, 16980-15-7; VIII, 16980-11-3; IX, 16980-12-4; XI, 16980-13-5; XII, 16980-14-6; vanadyl deoxophylloerythrin methyl ester, 15550-18-2; vanadyl deoxophylloerythroetioporphyrin, 17000-55-4.

Acknowledgment.—The authors thank Dr. A. Stoll for a generous gift of pheophytin.

(18) Reference 14, part II, p 199.

(19) A. Stern and H. Wenderlein, *Z. Physik. Chem.* (Leipzig), **174**, 81 (1935).

(20) The crystal structure of this material has been determined by R. C. Pettersen and L. E. Alexander, *J. Amer. Chem. Soc.*, **89**, 3873 (1968).