PORPHYRINS.

9.* NEW DATA ON THE POLYFORMYLATION OF METAL COMPLEXES OF ETIOPORPHYRIN I†

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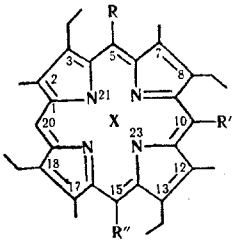
The structures of the products of the polyformylation of Cu, Ni, and Co complexes of etioporphyrin (EP) as monoformyl-, α,γ-diformyl-, α,β-diformyl-, and α,β,γ-triformyl-EP were established by electronic, IR, and PMR spectroscopy and mass spectrometry. α-Formyl-γ-(N-methylformaldimine)-EP and porphyrins that contain a cyclopentane ring can be formed by alkaline treatment of the Vilsmeier formylation products.

Studies of the formylation of metal complexes of porphyrins [1, 3, 4] have made it possible to establish the position of the formyl group in the final products [1]; however, the compounds formed during prolonged Vilsmeier formylation have not been analyzed in detail.

It was recently observed [5] that the Co complex of etioporphyrin I (Ia) is readily formylated to give a mixture of isomeric complexes of meso-diformyletioporphyrin I. Of course, the individual isomers of the porphyrins were not isolated, and their properties were not studied. It was reliably established in [6] that α,γ-diformyloctaethylporphyrin is also formed along with meso-monoformyloctaethylporphyrin in the formylation of the Cu complex of octaethylporphyrin under severe conditions in the presence of a large amount of the Vilsmeier reagent. Since no other formylporphyrins were detected, the authors concluded that the second formyl group electrophilically replaces the hydrogen atom in the most remote position — the γ position — of the porphyrin ring.

The aim of the present research was to ascertain the role played by the central metal atom in the direction and rate of polyformylation.



I a-m

I a X=Co, R=R′=R″=H; b X=2H, R=R′=R″=H; c X=Co, R=CHO, R′=R″=H; d X=2H, R=CHO, R′=R″=H; e X=2H, R=CHO, R′=H, R″=CHO; f X=2H, R=R′=CHO, R″=H; g X=2H, R=R′=R″=CHO; h X=Cu, R=R′=R″=CHO; i X=2H, R=CHO, R′=H, R″=CH=NMe; j X=Cu, R=CHO, R′=H, R″=CH=NMe; k X=Ni, R=CHO, R′=H, R″=CH=NMe; l X=Cu, R=R′=R″=H; m X=Ni, R=R′=R″=H

When we treated Ia with the Vilsmeier complex at 50°C for 2-3 min, in addition to the virtually quantitative formation of a mixture of isomeric Co complexes of meso-diformylporphyrins [5], we obtained a mixture of products that contains at least 20% of the Co com-

*See [1] for communication 8.
†See [2] for our preliminary communication.

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TABLE 1. PMR Spectra of Formylporphyrins*

Compounds I	Assignment of the PMR signals in ppm (δ scale)				
	CHO	meso-H	CH_2—CH_3	Ring CH_3	CH_2—CH_3
d	12,64 (1H)	9,92 (2H) 9,82 (1H)	3,92 (6H) q 3,76 (2H) q	3,48 (3H) [17], 3,46 (6H) [2, 12], 3,28 (3H) [7]	1,78 (3H) t 1,73 (3H) t 1,71 (3H) t 1,66 (3H) t
d†	12,45 (1H)	10,31 (2H) 10,27 (1H)	3,92 (6H) q 3,84 (2H) q	3,45 (3H) [17], 3,43 (3H) [12], 3,30 (3H) [2], 3,00 (3H) [7]	1,55 (3H) t 1,54 (3H) t, 1,50 (3H) t 1,45 (3H) t
e	12,43 (2H)	9,87 (2H)		3,47 (6H) [2.12], 3,27 (6H) [7, 17]	
e†	12,27 (2H)	10,13 (2H)	3,32 (4H) q 3,64 (4H) q	3,18 (6H) [2, 12], 2,91 (6H) [7, 17]	1,39 (6H) t 1,34 (6H) t
f	12,37 (1H) 12,30 (1H)	9,55 (2H)	3,90—3,20 (8H) m	3,31 (3H) [17], 3,30 (3H) [2], 3.18 (3H) [12], 2,99 (3H) [7]	1,80—1,35 (12H) m
f†	12,22 (1H) 12,19 (1H)	10,01 (2H)	3,80 (4H) q 3,63 (4H) q	3,32 (3H) [17], 3,16 (3H) [2], 2,90 (3H) [12], 2,57 (3H) [7]	1,45 (6H) t 1,35 (6H) t
g	12,17 (1H) 12,11 (1H) 12,06 (1H)	9,26 (1H)	3,47—3,20 (8H) m	3,19 (3H) [2], 3,03 (3H) [17], 2,83 (6H) [7, 12]	1,58—1,28 (12H) m
g†	12,03 (1H) 12,00 (1H) 11,97 (1H)	9,75 (1H)	3,50 (4H) q 3,25 (4H) q	3,05 (3H) [2], 2,81 (3H) [17], 2,49 (6H) [7, 12]	1,27 (6H) t 1,19 (6H) t
i	12,56 (1H) 10,43 (CH=N—)	9,92 (2H)	4,00—3,40 (8H) m	3,94 (3H), 3,45 (3H), 3,44 (3H), 3,26 (3H)	1,70—1,50 (12H) m 3,02 (3H, =N—CH_3)

*The numbering of the methyl substituents is indicated in brackets.

†These are the spectra obtained when trifluoroacetic acid was present.

plex of monoformyletioporphyrin I (Ic). We therefore increased the reaction time to 5-10 min, and the reaction products after hydrolysis of the reaction mixture with a saturated solution of sodium acetate and demetallation of the intermediate porphyrin complexes with concentrated sulfuric acid were subjected to repeated separation by means of preparative thin-layer chromatography (TLC) on a fixed layer of silica gel. As a result, we isolated four fractions, each of which differed appreciably with respect to the color of the band on the plate with silica gel and the color of the solutions in chloroform. In the order of decreasing R_f values, the colors of the bands on the plate varied as follows: the first fraction, with R_f 0.72, was grayish brown, the second fraction, with R_f 0.70, was lilac-colored, the third fraction, with R_f 0.54, was green, and the fourth fraction, with R_f 0.41, was yellow-green. In the case of hydrolysis of the formylation products, after evaporation of the solvent in vacuo, by means of aqueous alkali, in addition to the first four fractions, we isolated the most labile fifth fraction, the electronic spectrum of which was virtually identical to the spectrum of the porphyrin of the second fraction. All of the isolated compounds crystallized in the form of brown prismatic needles and, except for the porphyrin from fraction 5, had very similar IR spectra, in which an intense band at ∿1700 cm^{-1}, which corresponds to the carbonyl group of a formyl substituent in the meso position of the porphyrin ring, was present. The structures of the compounds isolated from each fraction were established unambiguously by PMR spectroscopy and were confirmed by data from the mass spectra.

It is apparent from the data from the PMR spectra (Table 1) that the compound of the first fraction corresponds to meso-monoformyletioporphyrin (Id), that of the second fraction corresponds to α,γ-diformyletioporphyrin (Ie), that of the third fraction corresponds to α,β-diformyletioporphyrin (If), and that of the fourth fraction corresponds to α,β,γ-triformyletioporphyrin (Ig). The signals of all of the protons are shifted to strong field as the number of formyl groups increases. The formyl groups have a particularly significant effect on the adjacent methyl substituents. We were therefore able to unambiguously assign the signals of the methyl protons for each of the four investigated porphyrins on the basis of the fact that the signals of the methyl group adjacent to the meso-formyl substituent

TABLE 2. Electronic Spectra of the Porphyrins

Compounds I	λ_{max}, nm ($\varepsilon \times 10^{-3}$)
e	411 (190), 512 (7,05), 550 (6,2) sh 581 (7,74), 646 (5,15), 666 (4,0) sh
f	424 (102), 546 (4,9) sh 611 (5,3), 691 (3,7)
f*	452 (163), 602 (6,6), 654 (5,3)
g	435 (103), 568 (5,2) sh 633 (6,7), 680 (5,3) sh
g*	471 (134), 633 (7,5), 693 (7,2)
i	411 (161), 511 (8,75), 549 (6,61), 581 (7,18), 642 (4,57), 666 (3,38) sh
j	407 (137), 423 (66,2) sh 539 (5,86), 573 (7,78), 646 (4,95)
j*	446 (100,6), 613 (6,1), 706 (8,7)
k	417 (95,4), 432 (97,7), 545 (5,28), 588 (6,94), 659 (11,1)
k*	450 (93,85), 643 (8,82), 737 (9,03)

*These are the spectra obtained when trifluoroacetic acid was present.

should be found at stronger field than the signal of a methyl group that is not shielded by an aldehyde residue. In the case of unsymmetrically substituted porphyrins If and Ig the protons of the formyl groups become nonequivalent and appear as singlets in the spectra. It is apparent from Table 1 that for unsymmetrically substituted porphyrins Id, f, g the contribution of each meso substituent to shielding of the protons of the aldehyde groups and the meso protons is additive and amounts to 26 and 33 Hz, respectively. In the case of symmetrically substituted porphyrin Ie the shift of the protons of the aldehyde groups and the meso protons is considerably smaller and is only 10 Hz. Protonation of the porphyrins by means of trifluoroacetic acid (TFA) leads to a certain increase in the ring current and a shift of all of the meso protons to weak field. Thus the PMR spectra of Id-g reflect the distortion of the porphyrin ring and the decrease in the ring current as a function of the number and position of the formyl groups in the porphyrin molecule.

The electronic spectra (Table 2 and Fig. 1a) are especially sensitive to the number and relative position of the formyl substituents in the porphyrin. The effect of the formyl groups is manifested most appreciably in the spectra of If, g, for which complete disappearance of the classical four-band spectrum in the visible region and considerable broadening and a bathochromic shift of the Soret band are characteristic; this is undoubtedly associated with disruption of the planar structure of the porphyrin ring. The dications of porphyrins (Fig. 1b) have characteristic two-band spectra that can be used for identification of the porphyrins.

The structures of porphyrins Id-g are also confirmed by data from the mass spectra. The presence of a molecular-ion peak and peaks of fragments due to detachment of CO groups is characteristic for all of these compounds (Table 3). Since porphyrins Ig undergo thermal decomposition in the ion source, we carried out the analysis of its Cu complex (Ih), in the spectrum of which the intensity of the molecular-ion peak is maximal.

In contrast to other isomeric porphyrins [7], the fragmentation of isomers If, e under electron impact differs markedly, and this can be used for their identification. Successive splitting out of two CO molecules is characteristic for the molecular ion of Ie and is accompanied by detachment of methyl and ethyl substituents from the porphyrin ring. If the elimination of a formyl group does occur, it does so only from the $[M - CO]^+$ fragment; however, the peaks of the resulting ions are superimposed on the peaks of the $[M - CO, - C_2H_5]^+$ fragments.

A characteristic feature of the mass spectrum of porphyrin If is the presence of an ion peak with m/e 507* ($C_{33}H_{39}N_4O$), which has the maximum intensity. The spectrum of the metastable ions obtained by the DADI method showed that this ion is formed from the $[M + 2]^+$ ion, the low-intensity peak of which is observed in the mass spectrum, and corresponds to detachment of a CHO group. Repeated rinsing of the ionization chamber with D_2O prior to recording of the spectrum of this compound did not lead to an increase in the intensity of the $[M + 2]^+$ ion peaks and to a corresponding shift in the m/e values of the fragments. The 505 and 506 ions are formed from the 534 molecular ion, the intensity of the peak of which may change considerably relative to the intensity of the $[M + 2]^+$ ion peak, depending on the recording conditions, as a result of elimination of CHO or CO groups. The subsequent frag-

*Here and subsequently, the numbers that characterize the ions are the mass-to-charge ratios.

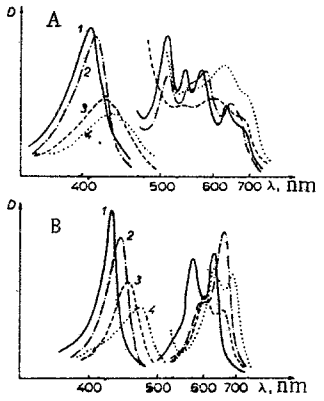


Fig. 1

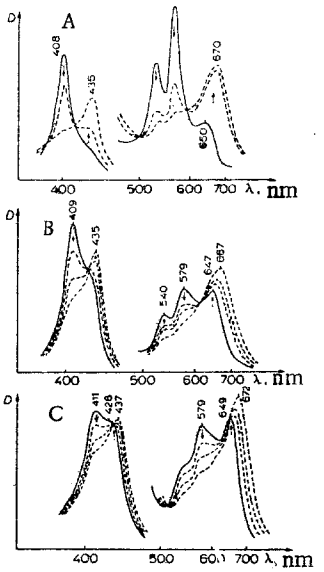


Fig. 2

Fig. 1. Electronic spectra of formylporphyrins: A) in chloroform; B) in chloroform + 1% trifluoroacetic acid; 1) Id; 2) Ie; 3) If; 4) Ig.

Fig. 2. Protonation of the Cu complexes of formylporphyrins in chloroform with added trifluoroacetic acid: A) Id; B) Ie; C) If.

TABLE 3. Mass Spectra of the Porphyrins

Compounds I	Empirical formula	m/e values (relative intensities, %)
d	$C_{33}H_{38}N_4O$	506 (M^+, 64), 478 (100), 463 (76), 449 (18), 433 (11)
e	$C_{34}H_{38}N_4O_2$	536 (M+2, 7), 535 (23), 534 (M^+, 48), 519 (7), 508 (15), 507 (39), 506 (92), 505 (30), 491 (38), 479 (47), 478 (100), 477 (50), 463 (40), 449 (21)
f	$C_{34}H_{38}N_4O_2$	536 (M+2, 14), 535 (7), 534 (M^+, 20), 508 (36), 507 (100), 506 (33), 505 (7), 491 (10), 479 (28), 478 (62), 477 (33), 463 (34), 449 (15)
h	$C_{35}H_{36}N_4O_3{}^{63}Cu$	623 (M^+, 100), 608 (12), 595 (26), 594 (22), 580 (7), 566 (12)
i	$C_{35}H_{43}N_5O$	549 (M+2, 66), 547 (M^+, 10), 534 (5), 532 (7), 519 (74), 504 (100), 490 (91), 488 (87), 478 (44), 475 (18), 463 (11), 460 (15), 445 (11)
j	$C_{35}H_{41}N_5O^{63}Cu$	608 (M^+, 35), 593 (12), 579 (88), 577 (100), 562 (13), 549 (34), 535 (11), 521 (14)
k	$C_{35}H_{41}N_5O^{58}Ni$	603 (M^+, 2), 575 (54), 545 (100), 529 (35), 515 (28)

mentation of the 505, 506, and 507 ions proceeds with detachment of CO, CHO, CH_3, and C_2H_5 particles.

Similar results were obtained in the formylation of the Cu and Ni complexes of porphyrin Ib for 3-5 h after separation of the reaction products (Table 4). In all cases the yield of isomer If was approximately double the yield of Ie. This fact is a direct indication that in the case of Ib complexes the direction of secondary electrophilic substitution is equally probable both in the adjacent β-meso position and in the opposite or γ position. An increase in the time of formylation of Ia to 15-20 min leads to an appreciable increase (up to 15-20%) in the yield of triformyl derivative Ig. All of these data constitute evidence that the intermediate phosphorus complexes formed as a result of the reaction actually exist in the "pseudoionic" form [8], which does not hinder the occurrence of the subsequent electrophilic substitution reactions. It should be noted that the Cu, Ni, and even Co complexes of the monoformyloctaalkylporphyrins do not undergo further formylation. The protonation of the Cu complexes of a number of formylporphyrins in the presence of TFA or dry HCl is shown in Fig. 2; an appreciable bathochromic shift of the Soret band is observed, the intensities of the α and β bands in the visible region decrease, and a new band appears

TABLE 4. Yields of Porphyrins As a Function of the Experimental Conditions

Starting complex	Reaction time, h	Temp., °C	Workup method	Porphyrin obtained (yield, %)
I l	0,5	50	A	Id (92)
I l	6	Reflux	A	Ie (24); If (43); Ig (5)
I l	4	„	B	Id (14); Ie (6); If (9); Ig (4); Ii (4)
I l	7	„	C	Id (22); VII+VIII (11)
I a	0,1	60	A	Ie (29); If (46); Ig (3)
I m	3	Reflux	A	Ie (30); If (46); Ig (3)

at 670 nm. This change in the electronic spectrum indicates transfer of positive charge from the aldehyde group to the porphyrin ring via the scheme

$$MP-CHO \xrightarrow{H^+} MP-CH=O^+-H \leftrightarrow [MP]^+=CH-OH,$$

where MP is the metalloporphyrin.

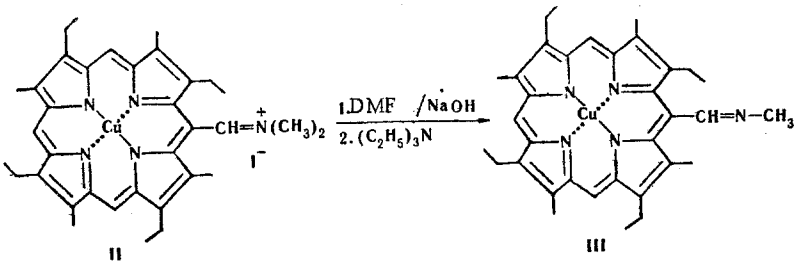
The positive charge, which is distributed over the entire porphyrin ring, prevents further electrophilic substitution reactions.

Two intense bands at 1695 and 1653 cm^{-1} are observed in the IR spectrum of the compound isolated from the fifth fraction, and this constitutes evidence for the presence of formyl and azomethine groups in the meso positions of the porphyrin ring. The presence of two singlet signals at 12.56 (CHO) and 10.43 ppm (CH=N—R) in the PMR spectrum of this compound confirms this conclusion. On the basis of the fact that the electronic spectra of the investigated compound and porphyrin Ie are virtually identical (Table 2), it was assumed that the two meso substituents are located in opposite α and γ positions. The ability of this porphyrin to undergo quantitative conversion to porphyrin Ie in chloroform in the presence of trace amounts of TFA and moisture was direct chemical evidence for this assumption.

The structure of the azomethine residue was established on the basis of an analysis of the mass spectrum (Table 3). Fragments with the compositions $C_{35}H_{43}N_5O$ and $C_{35}H_{41}N_5O$ correspond to the two peaks at 549 and 547 in the high m/e region according to data from the high-resolution mass spectrum. Since detachment of a molecule of CO is the most characteristic fragmentation for meso-formylporphyrins, the 519 fragment, which is formed from the 547 ion (DADI) and has the composition $C_{34}H_{41}N_5$ according to the data from the high-resolution mass spectrum, consequently is a porphyrin fragment that contains a meso CH=N—R substituent, and, proceeding from the m/e value of this fragment, it should be assumed that R = CH_3. The subsequent fragmentation of the 519 ion confirms this conclusion. As we have previously demonstrated [10], in the case of Schiff bases of meso-formyletioporphyrin the main fragmentation pathways lead to the following ions: $[M - CH_3]^+$, $[M - C_2H_5]^+$, $[M - R]^+$ and $[M - NH_2R]^+$. The 504, 490, and 488 fragments correspond exactly to fragmentation of the porphyrin with a —CH=N—CH_3 residue. On the basis of the facts set forth above, we assigned the α-formyl-γ-(N-methylformaldimine)etioporphyrin structure (Ii) to the compound from fraction 5. The presence of an azomethine group in the porphyrin is confirmed by the appearance in the electronic spectra of a long-wave band at 700 nm in the case of protonation of complexes Ij and Ik.

The presence in the mass spectrum of Ii of an intense $[M + 2]^+$ ion peak can evidently be explained by hydrogenation of the meso substituent during thermolysis of the porphyrin in the ionization chamber of the mass spectrometer, since the relative intensity of the 549 ion peak changes significantly from experiment to experiment, depending on the temperature in the ion source.

The formation of porphyrin Ii can be explained by reaction of the methylamine that is formed during alkaline hydrolysis of the Vilsmeier complex with the intermediate phosphorus complex with the formation of an azomethine group or dealkylation of the intermediate immonium salt to a Schiff base. For example, treatment of a solution of salt II in chloroform with dimethylformamide (DMF) that has been previously heated with aqueous alkali or treatment with anhydrous triethylamine leads to Schiff base III. It is therefore difficult to give an unambiguous answer to the question of the mechanism of the formation of porphyrin Ii.

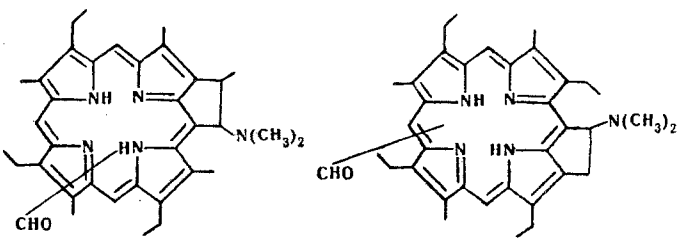


II III

In the preparation of meso-monoformylporphyrins the reaction mixture is usually heated with a saturated solution of sodium acetate at the end of the reaction. We repeatedly verified that replacement of the sodium acetate by aqueous alkali also leads only to metal complexes of the monoformylporphyrins, regardless of whether the solvent (usually dichloroethane) is or is not removed prior to the hydrolysis. However, large amounts of new products are formed when the reaction mixture is heated in the case of the formylation of the Cu and Ni complexes (Il and Im) under polysubstitution conditions. Thus refluxing the reaction mixture after formylation of complex Il with 10 N NaOH solution leads to a complex that, according to the data from the IR spectrum ($\nu_{C=O}$ 1700 cm^{-1}) and the electronic spectrum (a characteristic shoulder at ~650 nm), contained a meso-formyl group. The structure and composition of the substituents of the free porphyrin did not undergo any changes after demetallation of the complex with concentrated sulfuric acid; this was verified by reintroduction of copper into the porphyrin obtained and comparison with the starting Cu complex.

The appreciable decrease in the chromatographic mobilities on silica gel of both the Cu complex and the free porphyrin as compared with the known mono- and diformylporphyrins indicates the presence of a basic polar group in the unknown porphyrin. We were unable to establish the structure of the porphyrin by PMR spectroscopy because of the complexity of its spectrum; however, from the presence of two groups of meso protons it was ascertained that this porphyrin is a mixture of two isomeric forms in a ratio of 1:2.

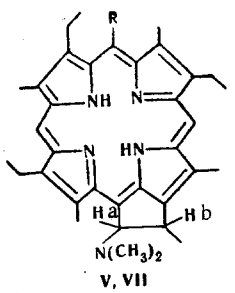
An analysis of the mass spectra of the porphyrin and its Cu complex (IV and IVa in the experimental section) indicates unambiguously that the 561 peak is due to the molecular ion, the elementary composition of which is $C_{36}H_{43}N_5O$, according to the data from the high-resolution mass spectrum. The most intense 516 and 517 ion peaks correspond to fragments with the compositions $C_{34}H_{36}N_4O$ and $C_{34}H_{37}N_4O$ and to detachment of C_2H_7N and C_2H_6N fragments from the molecular ion; this constitutes evidence for the presence of a substituent that contains an $N(CH_3)_2$ group in the porphyrin. We have previously established [10] that similar $[M - 44]^+$ and $[M - 45]^+$ fragments are characteristic for porphyrins and their metal complexes that contain a meso-dimethylaminomethyl group. Since there is no doubt that there is a formyl group in the porphyrin molecule, the 489 and 488 fragments correspond to detachment of CO from the 517 and 516 ions. The 489 fragment, the composition of which ($C_{33}H_{37}N_4$) differs, according to the data from the high-resolution mass spectrum, from that of Ib ($C_{32}H_{36}N_4$) only with respect to the presence of an additional carbon atom and the absence of a hydrogen atom, may suggest that porphyrin molecule IV contains a cyclopentane ring and can be represented in the form of structures A and B:



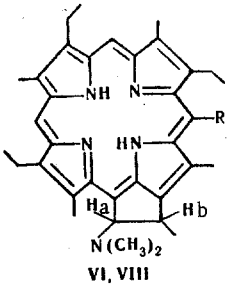
IVA IVB

After treatment of porphyrin IV with sodium borohydride, we were able to separate the corresponding hydroxymethyl derivative into two isomers by means of preparative thin-layer chromatography (TLC) on silica gel. The molecular ion peaks had m/e 563, and the second substituent consequently was not altered during reduction of the formyl group. The electronic spectra of the isomers (V and VI) were of the typical "phyllo" type; it is well-known that this is characteristic for porphyrins that contain a cyclopentane ring.

Only two singlets of meso protons were present in the PMR spectra of these protons, and this proved the individuality of each isomer. The presence in the spectra of doublets of methyl groups at δ 1.92 and 1.82 ppm and the corresponding quartets at 4.51 and 4.47 ppm of protons attached to the adjacent carbon atoms provides evidence for the formation of a cyclopentane ring through the meso substituent and the ethyl group. Since isomers Ie and If are formed in a ratio of 1:2 by the usual method of hydrolysis, we assume structure V for the isomer that is formed in smaller amounts and is more labile and structure VI for the other isomer. Consequently, the porphyrin that we isolated from the reaction mixture is a mixture of isomers VII and VIII.



V, VII



VI, VIII

V, VI R=CH_2OH;
VII, VIII R=CHO

The formation of a cyclopentane ring by intramolecular cyclization by alkaline treatment of the intermediate phosphorus complexes most likely occurs a) because of steric factors due to the presence of a second meso substituent and b) because of the accumulation of excess positive charge during tautomeric transformations of the immonium salts, which facilitates detachment of a proton from the methylene group of the ethyl substituent.

EXPERIMENTAL

The electronic spectra of solutions of the compounds in chloroform were recorded with a Specord spectrophotometer. The IR spectra of KBr pellets were recorded with a Perkin-Elmer 180 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ or $CDCl_3$ + 1% CF_3COOH were obtained with Varian HA-100D and Brucker WP-90 spectrometers with hexamethyldisiloxane as the internal standard. The mass spectra were obtained with a Varian MAT-311 spectrometer. Thin-layer chromatography was carried out on 20 by 20 cm plates with a fixed layer of Merck CF-254 silica gel.

General Methods for the Formylation of the Metalloporphyrins

Method A. A mixture of 100 mg of complex II and the complex obtained from 5 ml of dimethylformamide (DMF) and 6 ml of $POCl_3$ in 50 ml of dry dichloroethane was refluxed for 6 h, after which the solvent was removed in vacuo, and the residue was heated with 100 ml of a saturated solution of sodium acetate at 100°C for 1 h. The resulting precipitate was removed by filtration, dried, dissolved in chloroform, and chromatographed with a column filled with aluminum oxide to give 90 mg of a mixture of copper complexes of formylporphyrins, from which the free formylporphyrins were obtained by treatment with 20 ml of concentrated H_2SO_4 for 1 h after neutralization of the solution with aqueous alkali. Repeated chromatographic separation on plates coated with silica gel gave the individual porphyrins; Ie and Ii were recrystallized from chloroform, while the remaining porphyrins were recrystallized from chloroform–methanol.

Method B. The reaction mixture was evaporated in vacuo, and the residue was poured into 0.5 liter of water. The aqueous mixture was neutralized gradually with 10 N sodium hydroxide solution, and the precipitate was separated and chromatographed with a column filled with Al_2O_3 (elution with chloroform). The metal complexes of the porphyrins were worked up as in method A.

Method C. The reaction mixture upon completion of formylation was refluxed for 2 h with 100 ml of 10 N NaOH, and the organic layer was separated and evaporated in vacuo. The residue was chromatographed initially with a column filled with Al_2O_3 (elution with chloroform), and the principal fraction was purified additionally on plates coated with silica gel in a chloroform–methanol (10:1) system to give the Cu complex (IVa) of the porphyrin in the form of large prismatic crystals. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 406.5 (226), 534 (10.0), 569 (11.9), 645 hm (2.86) sh. Mass spectrum for $C_{36}H_{41}N_5O^{63}Cu$, m/e (%): 622 (M^+, 18), 607 (3), 577 (100), 562 (9), 549 (15), 548 (11). Porphyrin IV was obtained in 11%

yield from the Cu complex by demetallation and crystallization from chloroform–methanol. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 410 (151), 511 (9.1), 546 (4.54) sh, 575 (6.41), 627 (4.77), 650 sh; UV spectrum of the dication: 425 (213), 575 (9.3), 631 nm (10.85). Mass spectrum, m/e (%): 561 (M^+, 12), 546 (5), 517 (75), 516 (100), 501 (5), 489 (20), 488 (25), 473 (11), 459 (12). The conditions under which the reactions were carried out and the yields of the products are indicated in Table 4.

Preparation of $13^1,15^1$-Cyclo-13^1-methyl-15^1-dimethylaminomethyl-5-hydroxymethyl-3,8,18-triethyl-2,7,12,17-tetramethyl-21H,23H-porphine (V) and Its 10-Hydroxymethyl Isomer (VI). A 10-mg sample of a mixture of VII and VIII and 20 mg of $NaBH_4$ in 20 ml of tetrahydrofuran (THF) was heated at 40°C for 1 h, after which the solvent was removed by evaporation to dryness, and the residue was dissolved in chloroform and chromatographed repeatedly on plates coated with silica gel, as a result of which two fractions were isolated. Workup of the more labile fraction and crystallization of the residue from chloroform–methanol gave 2 mg of porphyrin V. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 410 (190), 510 (14.3), 546 (4.0), 573 (6.3), 625 (3.78); UV spectrum of the dication: 422 (258), 567 (13.2), 613 nm (8.8). Mass spectrum, m/e (%): 563 (M^+, 34), 548 (20), 533 (8), 519 (92), 518 (100), 503 (47), 502 (42), 489 (53), 475 (18). PMR spectrum, δ: 10.06 (1H), 9.95 (1H), meso-H; 6.73 (2H, CH_2OH); 4.51 (1H, q, J = 7.3 Hz, CH_b); 1.92 (3H, d, J = 7.3 Hz, CH_3–CH_b); 2.33 [6H, $N(CH_3)_2$]; 6.19 (1H, H_a); 3.68, 3.52, 3.53, and 3.48 (ring CH_3); −3.03 (1H), −3.32 ppm (1H), NH. Workup of the less labile fraction gave 3.5 mg of porphyrin VI. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 410 (190), 510 (14.0), 546 (5.2), 573 (6.4), 625 (6.6); UV spectrum of the dications: 422 (250), 567 (12.1), 613 nm (9.4). Mass spectrum, m/e (%): 563 (M^+, 15), 548 (7), 533 (5), 519 (93), 518 (100), 502 (30), 489 (15). PMR spectrum, δ: 10.03 (1H), 9.93 (1H), meso-H; 6.81 (2H, AB system, CH_2OH); 6.33 (1H, H_a); 4.47 (1H, q, J = 7.1 Hz, H_b); 1.82 (3H, d, J = 7.1 Hz, CH_3–CH_b), 3.74, 3.71, 3.62, and 3.46 (ring CH_3); 2.22 [6H, $N(CH_3)_2$]; −2.31 ppm (2H, NH).

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