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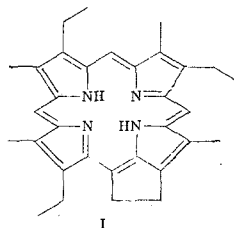
PORPHYRINS.

16.* THERMOLYSIS OF SCHIFF BASES OF MESO-FORMYLPORPHYRINS —

A CONVENIENT METHOD FOR THE SYNTHESIS OF PORPHYRINS

WITH A CYCLOPENTANE RING†

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A new general reaction involving the thermal decomposition of Schiff bases of meso-formyloctaalkylporphyrins, which leads to porphyrins that contain a cyclopentane ring, was discovered. The optimum conditions in the synthesis of porphyrins with substituted and unsubstituted cyclopentane rings were worked out in the case of the thermolysis of Schiff bases of meso-formyletioporphyrin I, meso-formyletioporphyrin II, and octaethylporphyrin. The synthesized compounds were characterized by data from the electronic, PMR, and mass spectra.

Porphyrins with a cyclopentane ring of the so-called [M — 2] series or the deoxophylloerythroetioporphyrin (I) series are widely represented in the porphyrin fractions of sedimentary rocks, petroleum oils, and shales. The origin of such porphyrins has not been rigorously established, although their presence in geological formations serves as the principal argument for the biogenic formation of "geological" porphyrins.


I

Up until now, very little has been known regarding the chemical and spectral properties of porphyrins with a cyclopentane ring because of the lack of convenient methods for the synthesis of such compounds. These syntheses are usually multistep processes, and the final product is isolated in low yield [4-6]. It is also unknown whether porphyrins with alkyl substituents in the cyclopentane ring, the synthesis of which has become possible only owing to our observed thermal intramolecular cyclization of Schiff bases [7], to the description of which this paper is devoted, exist in nature.

In an investigation of the mass spectra of aminomethylporphyrins II (R = H or CH₃, R¹ and R² = H or alkyl) we established [8] that the primary fragmentation of the molecular ions for these compounds proceeds with detachment of amine NHR¹R²; the possibility that fragment F₁ with an annelated cyclopentane ring is formed in this case was not excluded. In addition, an intense peak of an [M — NR¹R² + H]⁺ fragment (F₂) was observed in the mass spectra.

*See [1] for communication 15.
†See [2, 3] for preliminary communications.

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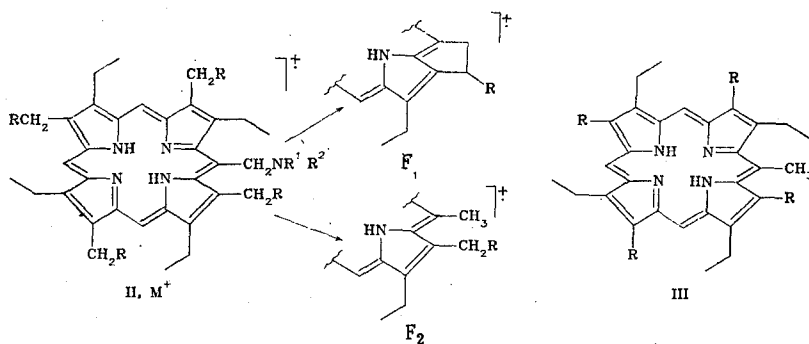
meso-Methylporphyrins III (R = Me or Et), which correspond to the F_2 fragment, are formed in 50-60% yields in the thermolysis of porphyrins II in vacuo. The desired porphyrins with cyclopentane rings were present in only trace amounts.

The molecular ions of Schiff bases of meso-formylporphyrins basically undergo fragmentation in the same way as meso-aminomethylporphyrins with the ejection of an amine, and we assumed that porphyrins with a cyclopentane ring, i.e., porphyrin IVa (M = 2H) from octaethylporphyrin derivatives and porphyrins Va and VIa (M = 2H) from etioporphyrin I derivatives, might be obtained by their thermolysis.
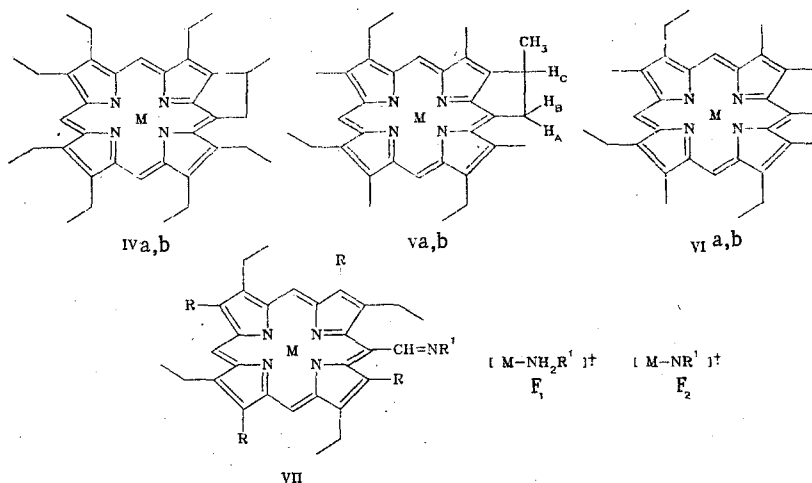
The presence in all of the investigated mass spectra of the Schiff bases (VII) of meso-formylporphyrins of intense peaks of ions that correspond to the F_2 fragment [8], which, as established by the DADI method, is not formed from the molecular ion and consequently is the product of thermal decomposition of the sample under the conditions of the mass-spectral experiments, served as a basis for this assumption.

The first experiments on the thermolysis of the Schiff bases of derivatives of meso-formyloctaethylporphyrin and meso-formyletioporphyrin I were conducted under conditions corresponding to the conditions of vaporization of the samples in the ionization chamber of the mass spectrometer, i.e., by sublimation in vacuo at $1 \cdot 10^{-3}$-$5 \cdot 10^{-5}$ mm (mercury column) ($1.5 \cdot 10^{-1}$-$6.5 \cdot 10^{-3}$ Pa) and 250-280°C. A copper complex (IVb), which, according to the mass-spectral data, corresponded to the expected F_2 fragment, was isolated from the products of sublimation of VII (R = Et, R^1 = CHMeEt, M = Cu) after chromatographic purification on silica gel. A porphyrin with composition $C_{37}H_{46}N_4$ (according to high-resolution mass-spectral data) was isolated in 46% overall yield based on starting complex VIIa after demetallation of complex IVb in concentrated H_2SO_4 and subsequent purification with a column packed with silica gel. With respect to the intensities of the bands and the position of λ_{max}, the electronic spectrum of the isolated porphyrin (see Table 1) was virtually the same as the spectrum of porphyrin I [4]. It follows from the PMR spectrum (see Fig. 1) that a methylcyclopentane ring is present in the analyzed porphyrin; the presence of a methyl group in the 3^1 position leads to characteristic coupling of all of the protons of the exo ring and their unambiguous interpretation, and porphyrin structure IVa can consequently be assigned to the isolated product. It should be noted that the protons of the methylene links in the unsubstituted cyclopentane ring form two unresolved multiplets [5].
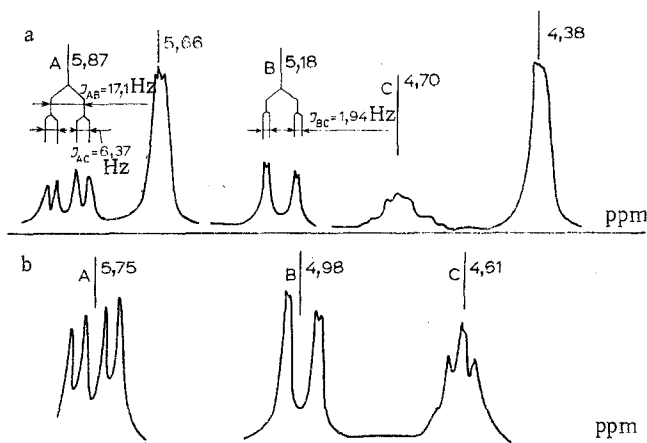
Fig. 1. PMR spectra of porphyrins in the region of the signals of the exo ring protons: a) inseparable mixture of isomers VIa + Va; b) IVa. The spectra were recorded in CDCl₃ with a WM-250 spectrometer with tetramethylsilane as the internal standard.

TABLE 1. Electronic Spectra of the Porphyrins

Com-pound	Solvent*	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)							
IV	A	400 (229)	500 (15,8)	534 (4,07)	563 (6,45)	616 (6,16)
IVa	A	403 (239)	503 (14,6)	538 (5,2)	566 (6,5)	518 (5,35)
	B	400 (286)	499 (15,7)	532 (4,5)	567 (6,7)	620 (7,6)
	C	400 (241)	502 (16,4)	537 (4,5)	568 (6,57)	621 (6,3)
	D	409 (392)	555 (16,1)	597 (5,8)		
IVb	A	402 (420)	528 (13,9)	565 (16,1)		
IVc	A	406 (371)	535 (13,8)	570 (12,0)		
	B	407 (315)	539 (13,8)	571 (11,5)		
Va+VIa	A	401 (215)	501 (14,3)	535 (5,1)	564,5 (6,2)	618 (6,0)
Vb+VIb	A	401 (430)	526 (15,5)	565 (18,7)		
XIV	A	401 (220)	501 (15,1)	535 (4,9)	565 (6,2)	618 (5,9)

*Solvents: A) Chloroform; B) chloroform—ether (1:3); C) benzene; D) chloroform + 1% CF₃COOH.

Because of its laboriousness and low efficiency, the thermolysis of Schiff bases by sublimation in a high vacuum does not make it possible to obtain significant amounts of porphyrins with cyclopentane rings. This is more a method for the formation of porphyrin IVa than a method for its production. In addition, we found that the most accessible starting complex VIIb (R = Et, R¹ = Me, M = Cu) can also be sublimed in a high vacuum without decomposition, which lowers the yield of porphyrin IVa appreciably and hinders its chromatographic purification.

We subsequently established that it is not necessary to maintain high-vacuum conditions and to strive for sublimation of the substance on the walls of the sublimator. Simple melting of the substance in vacuo at 0.1-3 mm (13-400 Pa) and 240-290°C (depending on the Schiff base used) is sufficient. The reaction is usually complete in 1-5 min, as judged from cessation of the evolution of gas bubbles (the amine) from the melt. In our opinion, a great advantage of this variant of the synthesis of porphyrins with a cyclopentane ring is the possibility of immediately obtaining a large amount of the desired porphyrin directly in a single experiment, since there is no limitation on the amounts of Schiff bases used for thermolysis.

Similar results were also obtained in the thermolysis of Schiff bases of meso-formyl-etioporphyrin I. In this case there was a possibility of cyclization through both the β-methyl and β-ethyl groups of the pyrrole rings. In fact, it is apparent from the PMR spectrum (see Fig. 1) of the product of thermolysis of VIIc (R = R¹ = Me, M = 2H) that the isolated porphyrin is a mixture of two isomers Va and VIa in a ratio of 1:2. Consequently, the formation of an unsubstituted cyclopentane ring through the meso substituent and the

adjacent β-methyl group is preferable to the formation of a methylcyclopentane ring with participation of the adjacent β-ethyl group. We were unable to separate isomers Va and VIa by chromatography because of their close mobilities. A mixture of isomers Va and VIa was also obtained by thermolysis of porphyrin VIId (R = Me, R^1 = cyclohexyl, M = Cu) to a mixture of products Vb and VIb (M = Cu) with subsequent demetallation with concentrated H_2SO_4 in 42% overall yield.

Thus the synthesis of a porphyrin that contains an unsubstituted cyclopentane ring without the admixture of other isomers can be realized only under the condition that the meso substituent is adjacent to two methyl groups. Schiff bases of meso-formyloctamethylporphyrin would be most suitable for this purpose, since only a single isomer (VIII) could be formed in this case. However, the low solubilities of metal complexes of octamethylporphyrin in dichloroethane markedly limit the possibility of obtaining Schiff bases via the Vilsmeier reaction and, consequently, the desired porphyrin VIII.
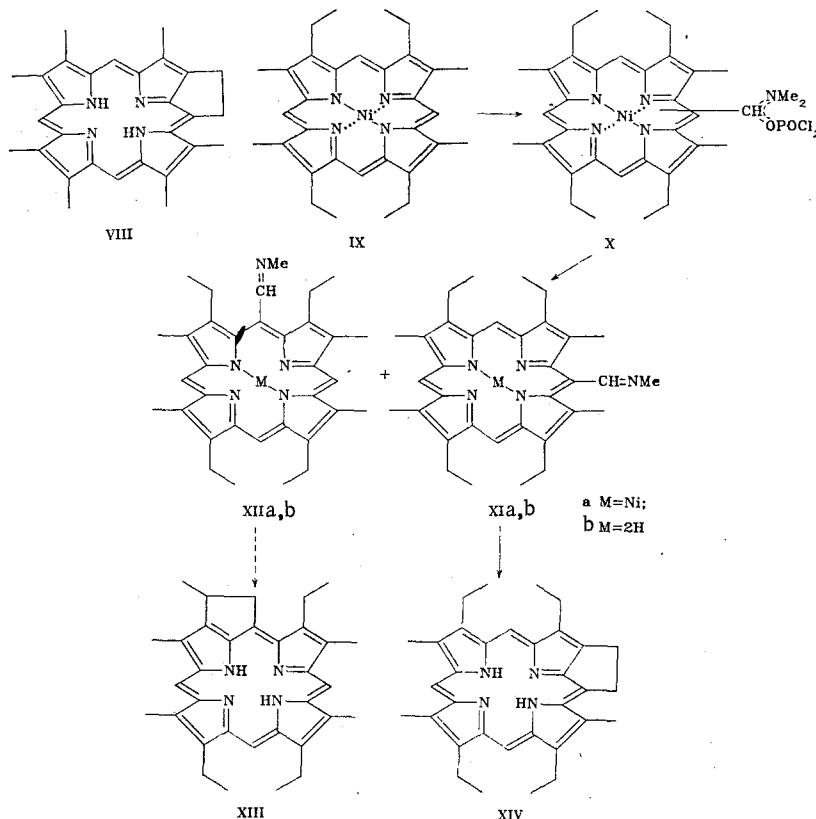

We therefore selected etioporphyrin II as the starting porphyrin, since the formylation of metal complexes of this compound via the Vilsmeier reaction takes place primarily in the β(δ) positions, and the formyl group in the final product is located between two methyl substituents. The formylation of the nickel complex (II) of etioporphyrin II, after treatment of intermediate "phosphorus complex" X with methylamine, gave a mixture of complexes XIa and XIIa in a ratio of 2:1, which we were able to separate into individual isomers by means of preparative thin-layer chromatography (TLC) on silica gel with subsequent demetallation to give free bases XIb and XIIb. In the thermolysis of the pure isomers we found that porphyrin XIIb does not melt up to 330°C and that when the temperature is raised further the corresponding porphyrin XIII is formed in low yield (5-10%), evidently because of profound destruction of porphyrins at high temperatures. Porphyrin XIV was obtained from isomer XIb via the standard method, and for its preparative synthesis we subjected a mixture of Schiff bases XIb and XIIb to thermolysis without chromatographic separation. According to PMR spectral data, a sample of XIV contained no more than 5-10% isomer XIII, which was not important for further physicochemical investigations.

A porphyrin with the composition $C_{37}H_{44}N_4$, which was also detected in trace amounts in the products of sublimation of porphyrin VIIe (R = Et, R^1 = Me, M = 2H), is formed along with other products as a result of thermolysis of Schiff bases of meso-formyloctaethyl-

porphyrin. The composition of this porphyrin corresponds to the F_1 fragment that is formed in the mass-spectrometric fragmentation of Schiff bases and has the maximum signal in the spectra.

The existing nomenclature of tetrapyrrole compounds recommended by the IUPAC rules [9] does not take into account the peculiarities of the designation of porphyrins with a substituted cyclopentane ring, and we therefore adopted the following principle for the designation of the substituents: For any depiction of a porphyrin with a cyclopentane ring the substituents are numbered in such a way that the exo ring is always located between the carbon atom in the 3^1 and 5^1 positions. The lowest ordinal number is required for the substituents in the exo ring in this case. The following (A) designations of the protons in porphyrin IVa, for which the chemical shifts and spin-spin coupling constants (SSCC) in the PMR spectra are presented in the experimental section, were adopted:
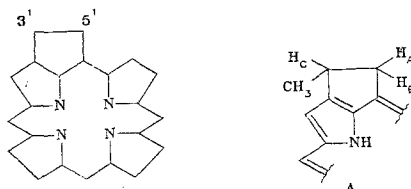
In conclusion, it should be noted that the mass spectra of isomeric porphyrins with substituted and unsubstituted cyclopentane rings are virtually identical. This means that porphyrins alkylated in the exo ring that are impossible to identify from the mass spectra may also be present among petroleum porphyrins of the [M − 2] series. The presence of such porphyrins in petroleum oils would serve as an argument in favor of the abiogenic formation of petroleum porphyrins, especially since the formation of a five-membered ring with the participation of β-alkyl substituents, as demonstrated in this research, is preferable in thermal transformations in the porphyrin series.

EXPERIMENTAL

The electronic spectra were recorded with Hitachi 320 and SF-18 (LOMO) spectrophotometers. The IR spectra of KBr pellets of the compounds were obtained with a Perkin-Elmer 180 spectrometer. The PMR spectra of solutions in $CDCl_3$ were obtained with Brucker WM-250 and WM-360 spectrometers with tetramethylsilane as the internal standard. The mass spectra were obtained with a Varian MAT-311 spectrometer. Chromatographic purification of the porphyrins was accomplished with columns packed with silica gel (100 × 400L, Czechoslovakia) and on 20 × 20 cm plates with a fixed layer (1 mm) of Merck CF-254 silica gel.

$3^1,5^1$-Cyclo-3^1-methyl-2,7,8,12,13,17,18-heptaethyl-21H,23H-porphin (IVa). General Method for the Thermolysis of Schiff Bases of meso-Formylporphyrins. A suspension of 500 mg (0.87 mmole) of porphyrin VIIe in 10 ml of chloroform was placed in an ampul (2.5 × 20 cm) and evaporated, and the residue was heated at 0.05-0.3 mm (mercury column) and 285-290°C on a Wood's metal bath for 4.5 min. It was then cooled, and the substance was dissolved in chloroform and chromatographed with a column (2.5 × 50 cm) packed with silica gel in a chloroform–carbon tetrachloride system (1:1). The principal fraction was separated and evaporated, and the residue was crystallized from chloroform–methanol to give porphyrin IVa. A 2.5-g sample of porphyrin VIIe gave 1.2 g (51%) or porphyrin IVa. PMR spectrum: 10.06, 10.02, and 10.01 (3H, all s, meso-H); 5.75 (1H, dd, J_{AB} = 16.7 Hz, J_{AC} = 6.8 Hz, H_A); 4.98 (1H, dd, J_{BC} = 2.0 Hz, H_B); 4.61 (1H, m, H_C); 4.12-4.18 (12H, CH_2CH_3); 4.02 (2H, q, CH_2CH_3); 2.04 (3H, d, J = 7.5 Hz, 3^1-CH_3); 1.83-1.97 (21H, CH_2CH_3); −2.9 and −3.68 ppm (2H, s, NH). Mass spectrum, m/z (%); 546 (M^+, 100), 531 (18), and 502 (10). The copper (IVb) and zinc (IVc) complexes of IVa were obtained by heating the porphyrin with the metal acetates in chloroform–methanol. Their electronic spectra are presented in Table 1.

$3^1,5^1$-Cyclo-7,13,17-trimethyl-2,8,12,18-tetraethyl-21H,23H-porphin (XIV). This compound was similarly obtained in 45-50% yield by thermolysis of a mixture of isomers rich in the XIb isomer. PMR spectrum (in $CDCl_3$ + 1% CF_3COOH): 10.54 (1H, s, meso-H); 10.46 (2H, s, meso-H); 5.63 (2H, m, 5^1-CH_2); 4.37 (2H, m, 3^1-CH_2); 4.09 (8H, overlapped q, CH_2CH_3); 3.63, 3.60, and 3.57 (9H, all s, ring CH_3); 1.91, 1.71, 1.68, and 1.66 (12H, all t, CH_2CH_3); −3.68 and −4.94 ppm (4H, NH). Mass spectrum, m/z (%): 490 (M^+, 100), 475 (21), 460 (5), 459 (5), and 445 (5).

$3^1,5^1$-Cyclo-2,3^1,7,12,17-pentamethyl-8,13,18-triethyl-21H,23H-porphin (Va) and $3^1,5^1$-Cyclo-8,13,18-trimethyl-2,7,12,17-tetraethyl-21H,23H-porphin (VIa). A mixture of isomers Va and VIa was formed in 45-50% yield in the thermolysis of porphyrin VIIc under similar conditions. Mass spectrum, m/z (%): 490 (M^+, 100), 475 (25), and 460 (5).

5-(N-Methylformaldimino)-3,7,13,17-tetraethyl-2,8,12,18-tetramethyl-21H,23H-porphin (XIIb) and 5-(N-Methylformaldimino)-3,7,13,17-tetramethyl-2,8,12,18-tetraethyl-21H,23H-porphin (XIb). A mixture of 102 mg (0.177 mmole) of complex IX and the complex from 1 ml of dimethylformamide (DMF) and 1.2 ml of $POCl_3$ was heated in 40 ml of dichloroethane at 50-60°C for 15 min, after which the mixture was cooled and treated with 40 ml of chloroform and 10 ml of a 25% aqueous solution of methylamine. The mixture was stirred for 10 min, and the organic layer was separated, washed with water, and filtered through a 5-cm layer of silica gel. The substance was eluted with chloroform, and the principal fraction was evaporated in vacuo to give 96 mg (89%) of a mixture of isomers XIa and XIIa. According to the results of TLC on Silufol and spectrophotometric determination, the XIIa/XIa ratio was 1:3.9, as compared with 1:1.3 in the mother liquor. PMR spectrum of complex XIa: 10.67 (1H, s, CH=N—Me); 9.53 (3H, s, meso-H); 3.83 q, 1.72 t (ring C_2H_5); 3.81 q, 1.69 t (ring C_2H_5); 3.39 and 3.16 (two s, ring CH_3); 3.89 ppm (3H, s, =N—CH_3). PMR spectrum of complex XIIa: 10.76 (1H, s, CH=N—Me); 9.52 (2H, s, meso-H); 9.50 (1H, s, meso-H): 3.80 q, 1.74 t, 3.64 q, 1.51 t (ring C_2H_5); 3.38 and 3.36 (two s, ring CH_3); 3.80 ppm (3H, s, =N—CH_3). Individual isomers XIa and XIIa were demetallated to XIb and XIIb with concentrated H_2SO_4. PMR spectrum of isomer XIb (in CF_3COOH): 10.78 (1H, s, CH=N—Me); 10.30 (3H, s, meso-H); 3.95-4.10 (ring (CH_2CH_3); 3.61 and 3.24 (two s, ring CH_3); 1.60 and 1.70 (two t, CH_2CH_3); −1.6 and −2.54 ppm (NH). Mass spectrum, m/z (%): 519 (M^+, 60), 504 (100), 490 (80), and 488 (80). PMR spectrum of isomer XIIb (in CF_3COOH): 10.32 (3H, s, meso-H); 4.43 (3H, s, =N—CH_3); 3.70-3.85 (CH_2CH_3); 3.40 and 3.10 (two s, ring CH_3); 1.51 and 1.48 (two t, CH_2CH_3); −0.42 and −0.61 ppm (4H, NH). Mass spectrum, m/z (%): 519 (M^+, 45), 504 (100), 490 (75), and 488 (80).

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