PORPHYRINS

11.* SYNTHESIS OF meso-METHYLPORPHYRINS

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UDC 547.749.07:543.51

The corresponding meso-methylporphyrins (in 40-50% yields) and porphyrins that contains a cyclopentane ring are formed by thermal sublimation in vacuo of meso-dimethylaminomethyletioporphyrin I and meso-dimethylaminomethyloctaethylporphyrin. When the Cu complex of meso-borinedimethylaminomethyletioporphyrin is heated at 200-210°C, it is converted, after demetallation, to meso-methyletioporphyrin in 75% yield. The UV, PMR, and mass spectra of the compounds obtained are presented.

Two brief communications regarding the synthesis of meso-methylporphyrins, which are of interest for the study of photosynthetic processes, were recently published [2, 3]. One of them deals with the cyclization of 1,19-unsubstituted biladienes-a,c in the presence of acetaldehyde acetal [2] to give the product in 28% yield, while the other [3] deals with the stepwise reduction of meso-formylporphyrin to the hydroxymethyl derivative by means of sodium borohydride, acetylation of the hydroxymethyl derivative, preparation of a zinc complex, catalytic hydrogenation on a palladium catalyst, and demetallation to give the product in an overall yield that does not exceed 60-65%. The direct methylation of the Pd complex of octaethylporphyrin with methyl fluorosulfonate [4] to give the product in 37% yield is also known. Very small amounts of meso-methylporphyrins are formed when meso-hydroxymethylporphyrins [5] are heated in dimethylformamide (DMF) in the presence of sulfuric acid. All of the methods described above are experimentally complicated, and the starting compounds are difficult to obtain.

In a study of the electron-impact mass spectra [6] of meso-dimethylaminomethylporphyrins and other N,N'-disubstituted aminomethylporphyrins [7-9] we established that the most characteristic ions in the mass spectra are the M^+, $[M - CH_2NRR'+H]^{+\cdot}$ (a), $[M - NRR'+H]^{+\cdot}$ (b), $[M-NRR']^+$ (c), and $[M-NHRR']^{+\cdot}$ (d) ions.

An analysis of the mass spectra of the metastable ions by the DADI method indicated unambiguously that the (a) and (b) ions are due to impurities rather than to fragments of the molecular ion. We assumed that these impurities are formed by thermal destruction of the meso-aminomethylporphyrins in the ionization chamber of the mass spectrometer to give unsubstituted porphyrin and meso-methylporphyrin, respectively.

In the case of fragment (d), which has the peak of maximum intensity in the mass spectra of many of the meso-aminomethylporphyrins that we have investigated, a stable porphyrin that contains a cyclopentane ring may correspond to it. This porphyrin could have been formed not only from the molecular ion but also by thermal cyclization with splitting out of an amine.

To verify these assumptions we investigated the structures of the products of vacuum sublimation of a number of meso-aminomethylporphyrins. We found that the sublimate from meso-dimethylaminomethyletioporphyrin (I) obtained at low vacuum [up to 10^{-1} mm (mercury column)] consists primarily of two porphyrins with the compositions $C_{32}H_{38}N_4$ (M 478) and $C_{33}H_{40}N_4$ (M 492), i.e., unsubstituted etioporphyrin (II) and meso-methyletioporphyrin (III), in 20-25 and 15-20% yields, respectively. A large amount of the substance undergoes resinification under these conditions. The yield of porphyrin III increases to 30-40% as the vacuum is increased (to 10^{-3}-10^{-5} mm), and the yield of porophyrin II decreases to 10-15%.

A small amount of a new porphyrin was detected in the case of separation of the sublimation products on plates with a fixed layer of silica gel. It had a small R_f value as compared with porphyrin and strong fluorescence in UV light as compared with meso-methylporphyrin III, which has virtually no fluorescence; this enabled us to obtain a pure sample after repeated separations. According to the data from the high-resolution

* See [1] for communication 10.

Institute of Biophysics of the Ministry of Public Health of the USSR, Moscow 123182. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 923-926, July, 1979. Original article submitted June 20, 1978.

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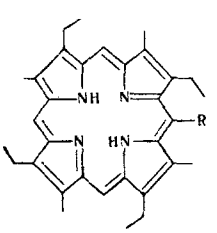
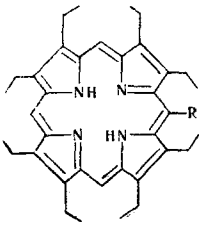


I–III, X, XII

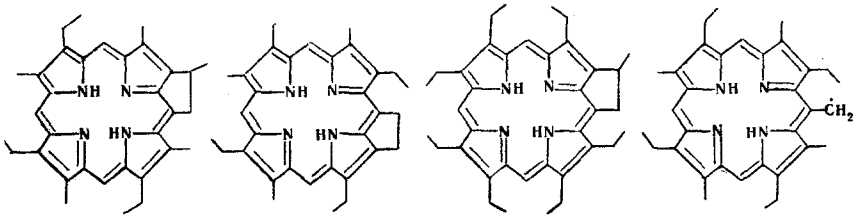


VI, VII

I, VI $R=CH_2N(CH_3)_2$; II $R=H$; III, VII $R=CH_3$; X $R=CH_2N(CH_3)_2 \cdot BH_3$; XII $R=CHDN(CD_3)_2$

mass spectrum, the molecular-ion peak of this porphyrin at m/e 490 had the composition $C_{33}H_{38}N_4$, which was in agreement with the composition of fragment (d), and its electronic spectrum of the "phyllo type" was also identical to the spectrum of the isomeric deoxophylloerythroetioporphyrin [10], which is a porphyrin that has a cyclopentane ring. Consequently, the assumption made above regarding the possibility of thermal intramolecular cyclization is confirmed.

The structure of the porphyrin obtained can be represented by isomeric forms IV and V, and the isolated substance is most likely a mixture of both forms. The amount of product obtained was insufficient for recording of the PMR spectrum.



IV V VIII IX

In the case of the thermolysis of meso-dimethylaminomethyloctaethylporphyrin (VI), in addition to meso-methyloctaethylporphyrin (VII), we also isolated a small amount of cyclic product VIII, which has an electronic spectrum that is similar to the spectra of porphyrins IV and V.

Thus the principal difference in the fragmentation of porphyrin I or VI during thermolysis and the fragmentation of the corresponding cation radical (the molecular ion) that is formed upon electron impact consists in the formation of mainly meso-methylporphyrin III and VII rather than porphyrins that contain a cyclopentane ring.

The thermolysis of aminomethylporphyrins probably proceeds via homolytic cleavage of the C–N bond and recombination of the resulting free radical IX with one of the hydrogen atoms contained in the side chain that is eliminated. An increase in the number of labile hydrogen atoms in the side chain consequently should lead to an appreciable increase in the yields of meso-methylporphyrins. In fact, porphyrin III was obtained in 40–50% yield when meso-borinedimethylaminomethyletioporphyrin X was sublimed, whereas porphyrin III was isolated in an overall yield of 75% after demetallation with concentrated sulfuric acid when its copper complex (XI) was fused. However, a mass-spectrometric analysis of porphyrin III, obtained by sublimation of deutero analog XII, showed that the hydrogen atom necessary for recombination of radical IX is furnished not only by the $\cdot N(CD_3)_2$ residue, but also by the entire molecule during the destruction of the substance (or from other sources), since the ions that contain one deuterium atom (the presence of a CH_2D group) rather than the two that were expected if the $\cdot N(CD_3)_2$ group were the hydrogen-atom donor give the maximum peak in the mass spectrum.

During a study of the mass spectra of a large number of porphyrins and their metal complexes that contain a $-CH_2X$ group (where $X = NH_2$, NHAlk, $NAlk_2$, or OAlk group) we arrived at the conclusion that, since they give fragment (c) in the fragmentation of the molecular ion, radical IX will be formed during thermolysis, and, as a result, the corresponding meso-methylporphyrin will be formed. In fact, sublimation of various substituted meso-aminomethylporphyrins obtained by reduction of the Schiff bases [12] and of a large number of meso-alkoxymethylporphyrins [13] and their complexes [14] leads to the corresponding meso-methylporphyrins in 30–40% yields.

EXPERIMENTAL

The electronic spectra of solutions of the compounds in chloroform were recorded with a Shimadzu MPS-50L spectrophotometer. The IR spectra of KBr pellets of the compounds were recorded with a Perkin-Elmer model 180 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Varian HA-100D spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were obtained with a Varian MAT-311 spectrometer. Preparative thin-layer chromatography (TLC) was carried out on 20 by 20 cm plates with a loose layer of Merck GF-254 silica gel in a chloroform–ether system (95:5). For column chromatography we used L100/160 silica gel and L40/250 aluminum oxide (Czechoslovakian SSR).

meso-Dimethylaminomethyloctaethylporphyrin (VI). A) A 100-mg sample of the copper complex of octaethylporphyrin was formylated by the method in [7] to give 120 mg of a crystalline "phosphorus complex," which was dissolved in 50 ml of methanol. Sodium borohydride (200 mg) was added, and, after 10 min, 10 ml of water was added gradually. The precipitated crystalline Cu complex of meso-dimethylaminomethyloctaethylporphyrin was removed by filtration, dried, and dissolved in 20 ml of chloroform. The chloroform solution was filtered through a layer (1 cm) of aluminum oxide, the filtrate was evaporated in vacuo with a rotary evaporator, and 10 ml of concentrated H_2SO_4 was added to the residue. The acid mixture was stirred for 1 h until the substance had dissolved completely, after which it was poured into 100 ml of water, and the aqueous mixture was neutralized to pH 4-5 with ammonium hydroxide. The substance was then extracted with chloroform, and the chloroform solution was filtered through a layer (1 cm) of aluminum oxide and chromatographed with a column filled with silica gel in a chloroform–methanol system (9:1). The principal fraction was collected and evaporated, and the residue was crystallized from chloroform–methanol to give 75-80 mg (75-80%) of meso-dimethylaminomethyloctaethylporphyrin. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 408 (140), 510 (9.15), 447 (6.42), 483 (5.30), 633 nm (2.12). IR spectrum: 2760 and 2810 cm^{-1}. Mass spectrum, m/e (%): 591 (M^+, 5), 548 (52), 547 (60), 546 (100), 533 (17), 532 (9), 531 (10), 517 (6), 503 (4), 58 (27).

B) A 120-mg sample of the "phosphorus complex" was ground in 5 ml of concentrated H_2SO_4 in a porcelain mortar. After 1 h, the mixture was poured into 100 ml of cold water, and the aqueous mixture was neutralized to pH 3-5 with sodium acetate. The porphyrin was extracted with chloroform, the extract was evaporated to 10-15 ml, 20 ml of methanol was added, and 200 mg of sodium borohydride was then added with stirring. After 1 h, the solution was evaporated, and the residue was dissolved in chloroform and chromatographed to give porphyrin VI in 85-90% yield.

d_7-meso-Dimethylaminomethyletioporphyrin (XII). This compound was obtained by the method in [8] by means of d_7-dimethylformamide for the preparation of the Vilsmeier complex. Mass spectrum, m/e (%): 542 (M^+,8), 493 (30), 492 (68), 491 (100), 490 (11), 479 (4), 478 (11), 477 (10), 476 (7). Mass spectrum of unlabeled I, m/e (%): 535 (M^+,10), 493 (15), 492 (50), 491 (78), 490 (100), 479 (10), 478 (22), 477 (20), 476 (15).

General Method for the Thermolysis of the Porphyrins. A 10-20 mg sample of the porphyrin was placed in a glass beaker with a height of 1.5 cm and a diameter of 1 cm, a few drops of chloroform were added, and the mixture was gradually evaporated in such a way that the substance was distributed in a uniform layer over the walls of the beaker. The beaker was placed in a 25-cm high test tube, and the test tube was evacuated to 10^{-3}-10^{-5} mm (mercury column); the test tube was then heated to 220-250°C from the end to a height of 5-7 cm. After cooling, the sublimate was extracted with chloroform, and the porphyrins were isolated by chromotography.

meso-Methyletioporphyrin (III). This compound, with R_f 0.75, was isolated in 15% yield from the sublimate of porphyrin I by chromatography. The fraction of the substance with R_f 0.40 corresponded to a mixture of porphyrins IV and V in 2-3% yield (by spectrophotometry). UV spectrum, λ_{max}, in ether: 499, 532, 566, 572, 593 sh, 610 sh, and 619 nm with a band intensity ratio of 1:0.32:0.43:0.37:0.13:0.15:0.49; in chloroform: 499, 532, 563, 589 sh, and 617 nm with a band intensity ratio of 1:0.24:0.39:0.09:0.41. Mass spectrum, m/e (%): 490 (M^+,100) , 475 (28), 462 (6), 461 (6), 460 (6), 445 (7). The substance with R_f 0.37 corresponded to porphyrin III, which was obtained in 40% yield. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 406 (170), 506 (16.0), 541 (4.9), 578 (4.9), 628 nm (1.2). According to the data in [11], λ_{max} ($\varepsilon \cdot 10^{-3}$): 406 (169.4), 506 (14.0), 539 (5.6), 576 (5.7), 627 nm (1.3). Mass spectrum, m/e (%): 494 (13), 493 (43), 492 (M^+,100), 491 (6), 479 (6), 478 (11), 477 (17), 462 (5), 467 (6). PMR spectrum, δ: 9.91 (2H), 9.73 (1H), meso-H; 4.44 (3H), meso-CH_3; 4.00 (4H), 3.98 (4H, q, j = 7.5 Hz, CH_2CH_3); 3.51 (6H), 3.46 (6H), ring CH_3; 1.77 (6H), 1.72 (3H), and 1.70 ppm (3H, t, j = 7.5 Hz, CH_2CH_3). Mass spectrum of meso-methyletioporphyrin obtained by sublimation of porphyrin XII, m/e (%): 495 (10), 494 (45), 493 (M^+,100) 492 (33), 479 (6), 478 (9), 477 (6), 462 (4), 447 (5).

meso-Methyloctaethylporphyrin (VII). Crystalline III (2-3% yield), with R_f 0.43, was isolated from the product of sublimation of porphyrin VI. UV spectrum, λ_{max}: 500, 532, 563, and 619 nm with a band intensity ratio of 1:0.35:0.38:0.40. Mass spectrum, m/e (%): 546 (M^+,100), 531 (18), 517 (18), 501 (10). The substance with R_f 0.40 (obtained in 45-50% yield) corresponded to meso-methyloctaethylporphyrin. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 406 (152), 507 (17.1), 542 (4.80), 579 (4.75), 628 nm (1.1). Mass spectrum, m/e (%): 548 (M^+, 100), 533 (25), 518 (7), 503 (10), 489 (9), 473 (6), 274 (35), 259 (12), 252 (8). PMR spectrum, δ: 9.93 (2H), 9.72 (1H), meso-H; 4.53 (3H), meso-CH_3; 4.02 q, 3.95 q (J = 7.5 Hz, CH_2CH_3); 1.83 t, 1.75 ppm t (CH_2CH_3).

Thermolysis of the Copper Complex (XI) of meso-Borinedimethylaminomethyletioporphyrin. A 100-mg sample of complex XI was heated slowly in a nitrogen atmosphere until the substance began to melt and gas evolution became vigorous (~200-210°C). After 2 min, the melt was cooled and dissolved in chloroform, and the solution was chromatographed with a column filled with silica gel. The principal fraction of the copper complex of meso-methyletioporphyrin was collected and evaporated, and the residue was dissolved in 10 ml of concentrated H_2SO_4. After 30 min, the solution was poured into 100 ml of cold water, and the aqueous mixture was neutralized with ammonium hydroxide. The porphyrin was extracted with chloroform, and the extract was filtered through a layer (1 cm) of aluminum oxide. The filtrate was evaporated, and the residue was crystallized from chloroform–methanol to give porphyrin III (75%), which, with respect to its chromatographic lability and spectral properties, was identical to porphyrin III obtained by sublimation.

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