PORPHYRIN

26.* SYNTHESIS OF NEW PORPHYRIN SYSTEMS, CYCLOPENTANE-PORPHYRIN LACTAMS. DOUBLE INTRAMOLECULAR CYCLIZATION OF SCHIFF'S BASES OF meso-FORMYLCOPROPORPHYRIN-I AND -II TETRAESTERS

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A new previously unknown double intramolecular cyclization has been discovered on thermolyzing nickel complexes of Schiff's bases of porphyrins containing propionic acid ester residues. This leads to the formation of cyclopentaneporphyrin lactams. Using coproporphyrin-I and -II derivatives as examples, the corresponding lactams were obtained, the structures of which were confirmed by PMR spectra using the nuclear Overhauser effect (NOE). A general scheme for the thermal decomposition of Schiff's bases of meso-formylporphyrins is proposed.

A new area of porphyrin investigation has developed in the last decade, viz., their use in medicine for the early diagnosis and photodynamic therapy of cancer. Mainly, water-soluble porphyrins and chlorins possessing the ability to accumulate selectively in cancer cells are used for these investigations.

In order to design water-soluble porphyrins with a cyclopentane ring possessing a more intense absorption in the red region of the spectrum than the usual octaalkyl substituted porphyrins, we extended our investigations on the thermolysis of Schiff's bases of meso-formyloctaalkylporphyrins [2] and β-formyl-meso-tetraalkylprophyrins [3] to porphyrins containing propionic ester residues.

The nickel complex of coproporphyrin-I tetraethyl ester (I) was chosen as the subject of the investigation. The corresponding complex (II) was obtained from it in 85% yield by the method of [4].

On thermolysis of complex (II) we hoped to obtain complex (III) and possibly complex (IV) if the thermolysis of porphyrins with propionic acid residues proceeded by the same mechanism as the thermolysis of Schiff's bases of the porphyrins investigated previously [2-5], i.e., according to Scheme 1.

On carrying out the thermolysis under standard conditions (6-10 min, 295-300°C, 0.05 torr) we discovered that two main products were formed which differed significantly in their chromatographic mobility on silica gel.

The mobile fraction was mainly the expected complex (III) contaminated with a small quantity of complex (I) and trace amounts of the cyclopentaneporphyrin (IV) and meso-methylcoproporphyrin-I (V) (according to PMR spectra). Complex (III) was isolated in 15-20% yield after further chromatographic purification of this fraction on a silica gel column. The free porphyrin (VI) was obtained in 90% yield by the demetallation of complex (III) in concentrated H_2SO_4. Hydrolysis of (VI) in 25% HCl gave the dihydrochloride of tetracarboxyporphyrin (VII) which was readily soluble in water as the appropriate salt.

The structure of the more polar main product, called by us "complex X," was established by combined analysis of its IR, PMR, and mass spectra.

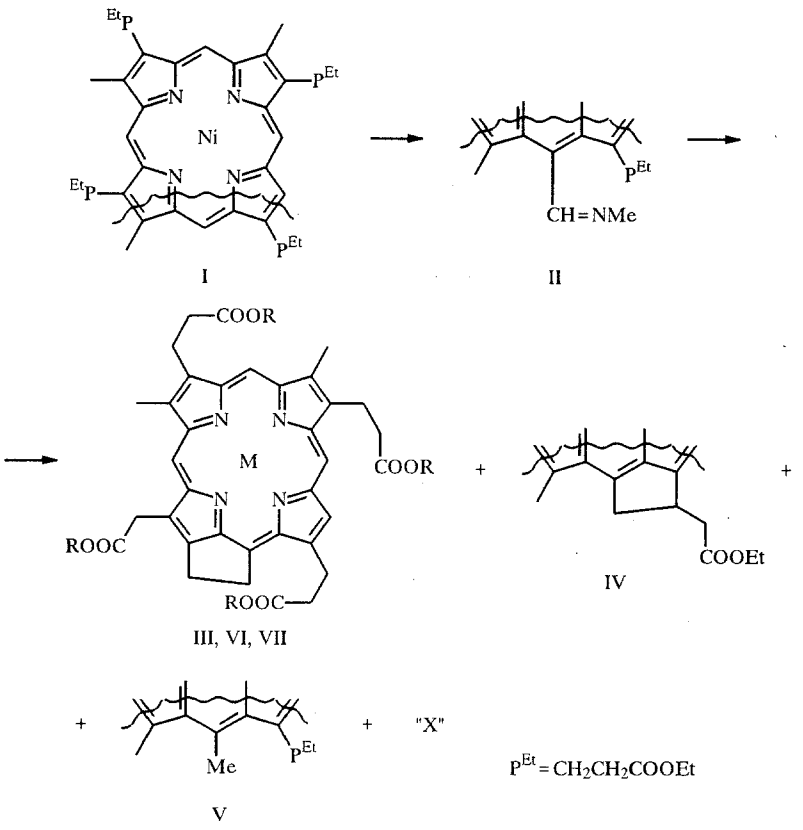
A characteristic feature of the PMR spectrum of "complex X" (see Fig. 1) was the presence of signals for only three ester groups, a doublet signal at 7.38 ppm, a complex multiplet at 5.03 ppm, a group of signals at 3.39-3.23 ppm, and a singlet

*For Communication 25, see [1].

Institute of Biophysics, Moscow 123182. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 180-188, February, 1993. Original article submitted May 19, 1992.

0009-3122/93/2902-0155$12.50

Scheme 1



III M = Ni, R = Et; VI M = 2H, R = Et; VII M = 2H, 2HCl, R = H

at 2.64 ppm. From the size of the chemical shift and coupling constant (5.4 Hz) the interactions between the signals at 7.38 ppm (H_x) and 5.03 ppm (H_y) were characteristics of vicinal cis-protons in porphyrins containing a disubstituted cyclopentane ring in which there is an electronegative substituent at position 15^1 and an alkyl substituent at position 13^1 [6]. It followed from double resonance data that, as for the cyclopentaneporphyrins investigated previously, the methyl group at position 12 is displayed as a doublet (J = 1.1 Hz) as a result of a homoallyl interaction with a proton of the cyclopentane ring [7]. On the other hand, the group of signals at 3.39-3.23 ppm is linked with the same proton which from its coupling constant may be assigned to a geminal proton of the CH_2 group at position 13^1 (J_{ab} = 17 Hz; J_{ay} = 9.9 Hz; J_{by} = 2 Hz).

It may be concluded from the odd mass number of the molecular ion peak in the mass spectrum of "complex X" that there are five nitrogen atoms present and elimination of a molecule of ethanol occurs on thermolysis of complex (II) (m/e 863). An intense band is observed at 1695 cm^{-1} in the IR spectrum of "complex X," which is absent from the spectrum of the initial Schiff's base, and which may be interpreted as the stretching vibration of an amide carbonyl group. Proceeding from these data

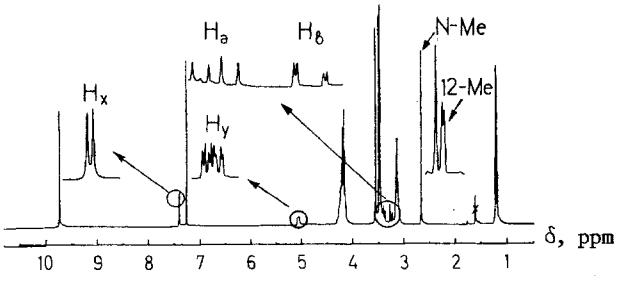
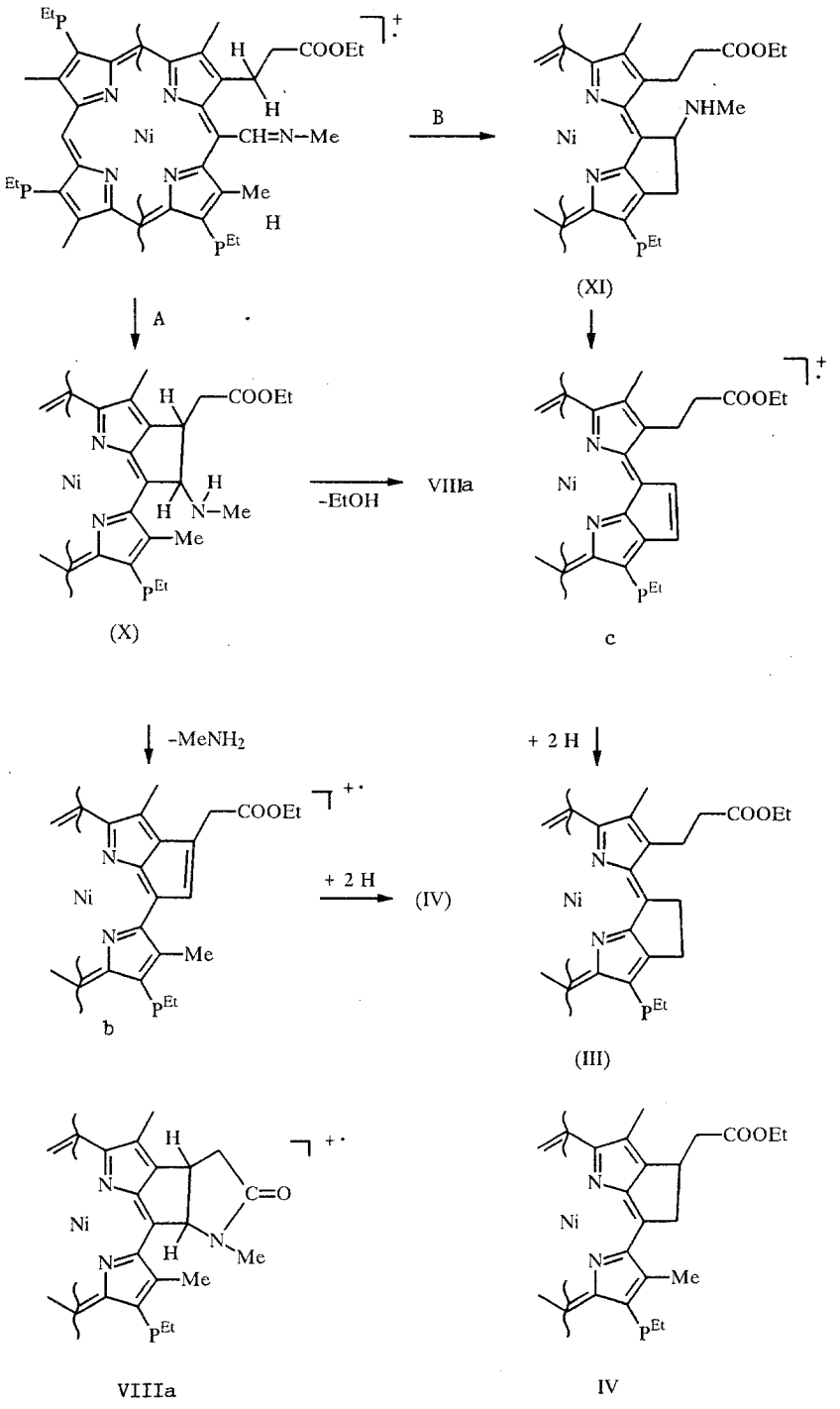


Fig. 1. PMR spectrum (360 MHz) of complex (VIII).

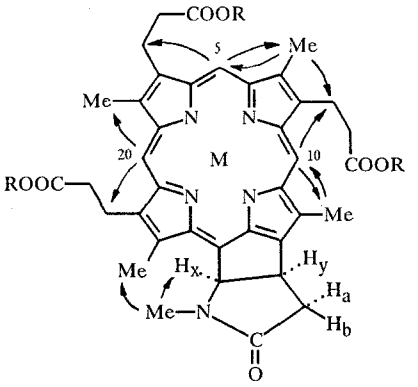
Scheme 2



the signal in the PMR spectrum at 2.64 ppm may be assigned to a CH_3 group on the amide nitrogen. The only possible structure for "complex X" corresponding to all the above data is the lactam structure (VIII) (see scheme on top of following page).

The close disposition of the amide methyl group to the ring methyl group in position 17 is evident from Dreiding models of the lactam (VIII). Further, from NOE data, intensification of the signal of the 17-CH_3 group at 3.53 ppm is observed on irradiating the singlet at 2.64 ppm. The signal at 7.38 ppm is intensified simultaneously which is additional confirmation of the formation of a lactam ring.

The lactam ring in compound (VIII) proved to be fairly stable. The free base of porphyrin (IX) was obtained in 80% yield on treating (VIII) with concentrated H_2SO_4 and all the main signals in the PMR spectrum were assigned by the NOE method as shown by the arrows in the structural formula.



VIII M = Ni, R = Et ("complex x"), IX M = 2H, R = Et, XXIV M = 2H · 2HCl, R = H

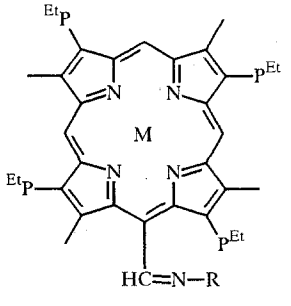
The visible region electronic spectrum of lactam (IX) retains all the features characteristic of known porphyrins with a cyclopentane ring. The only difference was an insignificant bathochromic shift of 1.5-2 nm and a significant increase in the intensity of the absorption for the first band at 620 nm.

The formation of lactams from the Schiff's bases of meso-formylporphyrins with propionic acid ester residues is important for explaining the thermolysis process and the mass-spectrometric decomposition of different Schiff's bases. It is now completely clear that the key point both in thermolysis and on decomposition of such porphyrins is the process of forming intermediate ions of the type of (X) or (XI) depending on the direction of cyclization (route A or B). In their turn the unstable intermediates (X) or (XI) undergo further conversions leading to the thermolysis products (III), (IV), (VIII), or the corresponding fragment ions (a, b, c) according to Scheme 2.

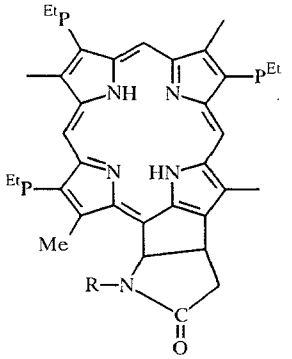
In order to confirm the overall character of the conversion discovered by us we carried out the thermolysis of the Schiff's bases of α-(β)-formylcoproporphyrin-II (XIV) nickel complex, since only one cyclization product (XV) or (XVI) can be formed from each isomer (XII) or (XIII) (see Scheme 3).

Vilsmeier formylation of complex (XIV) with subsequent treatment of the product (the so-called phosphorus complex) with aqueous methylamine gave a mixture of isomers (XII) and (XIII) in a 1:4 ratio (according to TLC and PMR spectra). The individual isomers (XVII) and (XVIII) were isolated by preparative TLC on plates with a bound silica gel layer and were used for preliminary experiments on thermolysis. The corresponding complexes of cyclopentaneporphyrins were detected in the thermolysis products of (XII) and (XIII) and differed significantly in chromatographic mobility on silica gel. As a result of this the mixture of Schiff's bases (XII) and (XIII), obtained by formylation, was used directly for the thermolysis and the preparation of cyclopentaneporphyrins in preparative quantities. The thermolysis products (XV) and (XVI) were isolated by column chromatography on silica gel. Their structures were confirmed by PMR and mass-spectral data.

The Schiff's bases of meso-formylporphyrins with primary amines other than methylamine may be used for the synthesis of cyclopentaneporphyrins which enables porphyrins with various substituents on the amide nitrogen to be prepared. For example, the lactams (XXI) and (XXII) were synthesized from the complexes (XIX) and (XX).



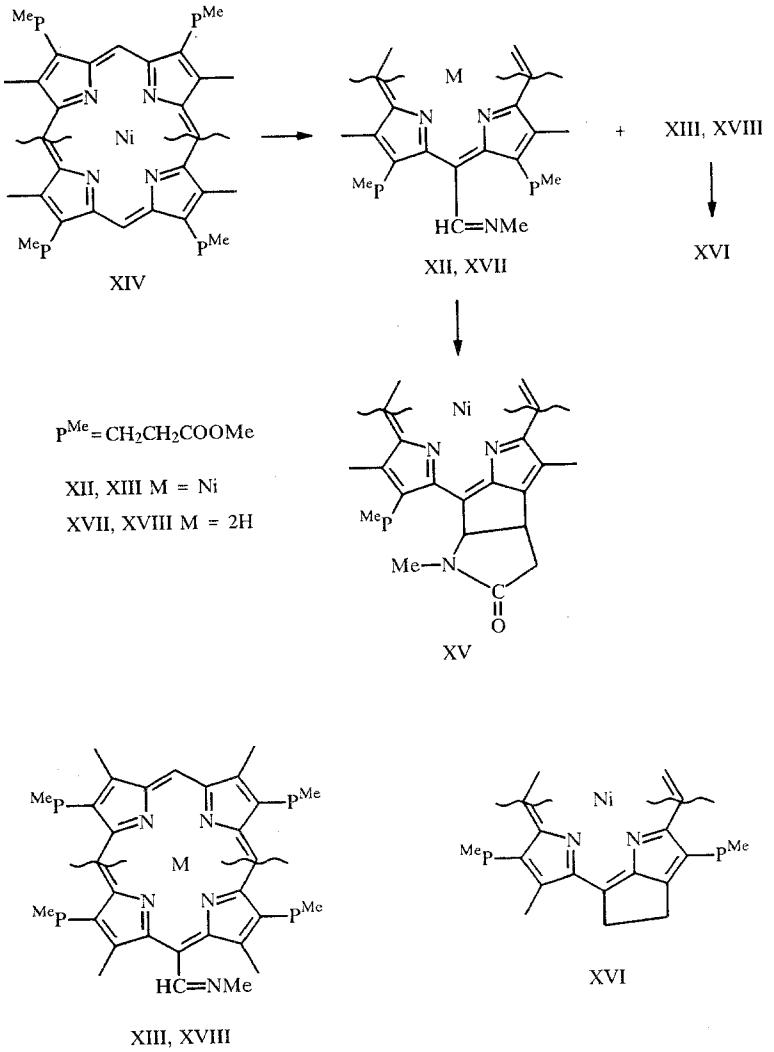
XIX, XX



XXI–XXIII

XIX, XXI R = CH_2Ph; M = Ni; XX, XXII R = CH_2CH_2Ph, M = Ni;
XXIII R = CH_2CH_2Ph, M = 2H

Scheme 3



Replacement of the methyl substituent on the amide nitrogen by a phenylalkyl substituent (CH_2Ph) or (CH_2CH_2Ph) leads to a certain complexity of the PMR spectra as a result of the protons of the amide substituent with complete retention of the basic features characteristic of the H_x, H_y, H_a, and H_b protons of the lactam (VIII). Due to conformational and steric interactions and the effect of the porphyrin ring current each of the protons of the CH_2 group of the phenyl substituent appear as separate multiplets. For compounds (XXI) the CH_2-Ph group is observed at low field due to the phenyl ring swinging away from the porphyrin macrocycle. The multiplets of the CH_2-CH_2-Ph group appear at high field due to its location above the plane of the porphyrin and the shielding effect of the ring current. For the same reason the ortho-protons of the phenyl ring are shifted by 0.8 ppm toward high field compared with the analogous signals in phenylethylamine.

To obtain water-soluble porphyrins we carried out an acid hydrolysis of porphyrin (IX) in hydrochloric acid and obtained the corresponding triacid (XXIV) in high yield with retention of the lactam ring. This compound was readily soluble in water as the trisodium salt.

It is evident from the data presented that the thermolysis of Schiff's bases of meso-formylporphyrins with propionic ester residues is a promising new direction for creating a great variety of water-soluble porphyrins containing additional exocycles in the molecule.

EXPERIMENTAL

Electronic spectra were taken on Beckman UV-5270 and Hitachi model 320 spectrophotometers. The PMR spectra were taken on a Bruker WM-360 instrument, internal standard was TMS. Mass spectra were recorded on Varian MAT-311 and MAT-44 instruments. The chromatographic purity of porphyrins was checked on columns of silica gel 40 × 100 (Czechoslovakia), preparative TLC was carried out on plates (20 × 20) with a bound layer of silica gel type GF_{254} (Merck) of 1 mm thickness.

The data of elemental analysis for C, H, and N corresponded to the calculated values.

Nickel Complex of 3,7,13,17-Tetra-(2-ethoxycarbonylethyl)-5-(N-methyliminomethyl)-2,8,12,18-tetramethyl-21H,23H-porphyrin (II), ($C_{44}H_{52}N_4NiO_8$). **A.** Nickel complex of coproporphyrin-I tetraethyl ester (I). A solution of nickel acetate (0.5 g) in AcOH (10 ml) was added to a solution of coproporphyrin-I tetraethyl ester (0.5 g) in DMF (50 ml) at 100°C, the mixture boiled for 5 min, cooled, and AcOH (10 ml) added with stirring. The crystalline precipitate of complex (I) was filtered off, washed with methanol, and dried to give complex (I) (0.5 g: 87%). UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 401 (228), 520 (5.26), 557 nm (16.05). PMR spectrum: 9.71 (4H, s, meso-H); 4.18 (8H, t, $C\underline{H}_2CH_2CO$); 3.43 (12H, s, CH_3-ring); 4.10 (8H, q, $C\underline{H}_2CH_3$); 3.08 (8H, t, $CH_2C\underline{H}_2CO$); 1.2 ppm (12H, t, $CH_2C\underline{H}_3$).

B. Complex (I) (1 g) and dichloroethane (70 ml) were added to the Vilsmeier complex from $POCl_3$ (3.6 ml) and DMF (6 ml) and the mixture heated for 40-50 min at 70-75°C until disappearance of the initial complex. The solvent was removed in vacuum and crushed ice (100 g) added to the oily residue with vigorous stirring. The solid was filtered off, dissolved in chloroform (150 ml), and a 25% aqueous solution (20 ml) of methylamine added. The solution was shaken for 10 min, washed with water, the organic layer separated, and chromatographed on a column of silica gel in chloroform. The main fraction was evaporated in vacuum and complex (II) (860 mg: 78%) was obtained after crystallization from chloroform–methanol. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 407 (200), 526 (10.0), 563 nm (19.3). PMR spectrum: 10.71 (1H, q, J = 1.4 Hz, CH=N–); 9.56, 9.55 (2H, 1H, all s, meso-H); 4.27, 4.17-4.14 (14H, q, m, 4 × $C\underline{H}_2CH_3$, 3 × $C\underline{H}_2CH_2CO$); 3.95 (2H, t, $C\underline{H}_2CH_2CO$); 3.42, 3.41, 3.40, 3.17 (all s, CH_3-ring); 3.11, 3.09, 3.03, 2.84 (all t, 4 × $CH_2C\underline{H}_2CO$); 3.84 (d, J = 1.4 Hz, N–CH_3); 1.32, 1.21, 1.18, 1.17 ppm (all t, 4 × $CH_2C\underline{H}_3$). Mass spectrum, m/e (%): 863 (M^+, 19), 848 (7), 836 (54), 834 (76), 832 (64), 822 (100), 817 (28).

2,7,12,17-Tetra-(2-ethoxycarbonylethyl)-3,8,18-trimethyl-13^1,15^1-cyclo-21H,23H-porphin (VI) and 3,8,18-Tri-(2-ethoxycarbonylethyl)-2,7,12,17-tetramethyl-13^1,15^1-cyclo-13^1-carboxymethyl-15^1-(N-methylamino)-21H,23H-porphin Lactam (IX). Complex (II) (860 mg) was heated in vacuum (0.05 mm Hg) at 295-300°C for 10 min. After cooling, the thermolysis product was dissolved in chloroform (10 ml) and chromatographed on a column of silica gel (4 × 25 cm) in CCl_4–ether (4:1). After removing the mobile zone (fraction 1) chromatography was continued with chloroform–acetone (95:5) until elution of the main zone of the more polar compound (fraction 2).

Fraction 1 was chromatographed again on a column of silica gel in chloroform–ether (95:5). Initially a mixture of complexes (II) and (V) (40 mg) was eluted and then the main compound (III) (146 mg: 17%). UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 393 (200), 514 (13.1), 552 nm (24.2). PMR spectrum of (III) (7.00 mg in 0.5 ml $CDCl_3$); 9.60, 9.56, 9.44 (all s, 5-, 20-, 10-H); 4.63 and 3.52 (two m, 15^1-CH_2, 13^1-CH_2); 4.25-4.20, 1.29, 1.27, 1.20 (m, three t, 3 × C_2H_5); 4.17 (t, 2^1-, 7^1- 2 × CH_2), 3.97 (t, 12^1-CH_2), 3.90 (t, 17^1-CH_2); 3.43, 3.406, 3.36 (all s, 3-, 8-, 18-CH_3); 3.12, 3.08, 2.82 ppm (overlapping t, 4 × CH_2CH_2CO). Mass spectrum, m/e (%): 834 (M^+, 100), 822 (15), 761 (10), 747 (24), 678 (35), 664 (39).

Complex (VIII) (262 mg: 32%) was obtained from fraction 2 after a further chromatographic purification on a column of silica gel in chloroform–acetone (95:5) and crystallization from chloroform–methanol. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 394 (165), 517 (10.9), 554 nm (26.8). PMR spectrum: 9.72 (s, meso-H); 7.38 (1H, d, H_x, J_{xy} = 5.4 Hz); 5.03 (1H, m, H_y); 4.26-4.15 (12H, m, 3 × $C\underline{H}_2CH_2CO$, 3 × $C\underline{H}_2CH_3$); 3.53, 3.48, 3.45 (all s, 3 × CH_3-ring), 3.44 (3H, d, J = 1.1 Hz, 12-CH_3); 3.39 (1H, d.d, H_a, J_{ab} = 17 Hz, J_{ay} = 9.9 Hz); 3.23 (1H, d.d, J_{ab} = 17 Hz, J_{by} = 2 Hz, H_b); 3.13-3.10 (6H, m, 3 × $CH_2C\underline{H}_2CO$); 2.64 (3H, s, N–CH_3); 1.19, 1.18, 1.17 ppm (all t, 3 × $CH_2C\underline{H}_3$). Mass spectrum, m/e (%): 817 (M^+, 100), 730 (27).

Porphyrin (VI) was obtained in 90% yield by the demetallation of complex (III) in concentrated H_2SO_4. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 402 (193), 500 (15.7), 534 (3.79), 565 (6.13), 616 nm (4.67). PMR spectrum: 10.01, 10.00, 9.97 (all s, meso-H); 5.35, 4.07 (2 m, CH_2CH_2-exocyclic); 4.46-4.33 (overlapping t, 4 × $C\underline{H}_2CH_2CO$); 4.24-4.17 (overlapping q, 4 × $C\underline{H}_2CH_3$); 3.69; 3.68, 3.58 (all s, CH_3-ring); 3.40, 3.28, 3.23, 3.10 (all t, 4 × $CH_2C\underline{H}_2CO$); 1.28, 1.26, 1.20, 1.17 (all t, 4 × $CH_2C\underline{H}_3$); –3.02, –3.77 ppm (two s, NH). Mass spectrum, m/e (%): 778 (M^+, 100), 691 (22). Found, %: C 69.4; H 7.0; N 7.2. $C_{45}H_{54}N_4O_8$. Calculated, %: C 69.4; H 7.0; N 7.2.

Porphyrin (IX) was obtained in 85% yield by the demetallation of complex (VIII) in concentrated H_2SO_4. UV spectrum, λ_{max} ($\varepsilon \cdot 10^{-3}$): 403 (189), 502 (14.9), 535 (4.9), 566 (6.05), 619 nm (7.68). PMR spectrum: 10.07, 10.05, 9.99 (all s, 20-H, 5-H, 10-H); 7.51 (d, H_x, J = 5.4 Hz); 5.00 (m, H_y); 4.42, 4.40, 4.32 (all t, 18-, 8-, 3-$C\underline{H}_2CH_2CO$); 4.18, 4.15, 4.13 (all q, 3 × $C\underline{H}_2CH_3$); 3.66, 3.64, 3.58 (all s, 7-, 17-, 2-CH_3); 3.56 and 3.48 (d, J = 1.2 Hz and m, 15^1-CH_2); 3.25-3.22 (overlapping t, 3 × $CH_2C\underline{H}_2CO$); 2.75 (s, N−CH_3); 1.19, 1.16, 1.14 (all t, 3 × $CH_2C\underline{H}_3$); −3.05, −3.98 ppm (two s, NH). Mass spectrum, m/e (%): 761 (M^+, 100), 716 (14), 689 (10), 688 (14), 674 (34).

3,7,13,17-Tetra-(2-methoxycarbonylethyl)-2,8,12,18-tetramethyl-15-(N-methyliminomethyl)-21H,23H-porphin (XVII) and 2,8,12,18-Tetra-(2-methoxycarbonylethyl)-3,7,13,17-tetramethyl-15-(N-methyliminomethyl)-21H,23H-porphin (XVIII). A mixture (180 mg: 85%) of isomers of the nickel complexes (XII)/(XIII) was obtained by Vilsmeier formulation of complex (XIV) (200 mg) by the method given above for compound (II). Found, %: C 62.3; H 6.0; N 8.4. $C_{42}H_{47}N_5NiO_8$. Calculated, %: C 62.4; H 5.9; N 8.7.

A mixture of isomers (XVII)/(XVIII) was obtained in 80% yield by the demetallation of complexes (XII)/(XIII) (50 mg) in concentrated H_2SO_4 after crystallization from chloroform−methanol. Samples of the individual isomers were isolated by preparative TLC on silica gel plates in chloroform−acetone (95:5) for the nickel complexes and in chloroform−methanol for the free porphyrin bases. Compounds (XII) and (XVII) possess a higher chromatographic mobility than compounds (XIII) and (XVIII).

Isomer (XII). UV spectrum, λ_{max} (relative intensity): 399 (16.1), 523 (1.0), 560 (1.91). PMR spectrum: 10.68 (1H, br.s, CH=N−); 9.49 and 9.47 (1H, 2H, two s, meso-H); 4.14, 3.88, 3.11, 2.88 (two s, CH_3-ring and $COOCH_3$); 3.74 ppm (d, J = 1.4 Hz, N−CH_3). Mass spectrum, m/e (%): 807 (M^+, 13), 776 (M − NH_2Me, 51), 775 (M − MeOH, 100), 765 (5), 719 (16).

Isomer (XIII). UV spectrum, λ_{max} (relative intensity): 398 (15.9), 522 (1.0), 558 (2.04). PMR spectrum: 10.61 (1H, br.s, CH=N−); 9.56, 9.53 (2H, 1H, two s, meso-H); 4.16, 3.10, 3.05 (m, t, t, $C\underline{H}_2C\underline{H}_2CO$); 3.89 (d, J = 1.4 Hz, N−CH_3); 3.69, 3.66, 3.40, 3.16 (all s, CH_3-ring and $COOCH_3$). Mass spectrum, m/e (%): 807 (M^+, 33), 792 (23), 780 (95), 778 (100), 776 (90).

Isomer (XVII). UV spectrum, λ_{max} (relative intensity): 404 (11.58), 503 (1.0), 537 (0.52), 574 (0.42), 626 nm (0.25). PMR spectrum: 10.80 and 3.98 (1H and 3H, q, d, J = 1.8 Hz, CH=N−CH_3); 10.10, 9.96 (2H and 1H, two s, meso-H); 4.05 and 3.27 (4H, 4H, two t, 2 × CH_2CH_2CO); 4.02 and 2.94 (t, m, 2 × CH_2CH_2CO); 3.80, 3.66, 3.63, 3.59 (all s, CH_3-ring and $COOCH_3$; NOE 10.10 → 3.63 and 3.59); −3.41 ppm (2H, s, N−H). Mass spectrum, m/e (%): 751 (M^+, 14), 720 (95), 719 (100), 710 (25), 678 (35), 664 (52).

Isomer (XVIII). UV spectrum, λ_{max} (relative intensity): 403 (12.45), 502 (1.0), 534 (0.51), 572 (0.42), 624 nm (0.195). PMR spectrum: 10.75 and 4.13 (1H and 3H, q, d, J = 1.8 Hz, −C<u>H</u>=N−C<u>H</u>$_3$); 10.13 and 9.99 (2H, 1H, two s, meso-H); 4.41, 4.409, 3.28, 3.21 (all m, 4 × $C\underline{H}_2C\underline{H}_2CO$); 3.67, 3.66, 3.61, 3.28 (all s, CH_3-ring and $COOCH_3$; NOE 3.61 → 9.99); −3.46 ppm (2H, s, NH). Mass spectrum, m/e (%): 751 (M^+, 12), 722 (50), 720 (100), 710 (90).

Nickel Complexes of 3,7,17-Tri-(2-methoxycarbonylethyl)-2,8,12,18-tetramethyl-13^1,15^1-cyclo-13^1-(carboxymethyl)-15^1-N-methylamino-21H,23H-porphin Lactam (XV) and 2,8,12,18-Tetra-(2-methoxycarbonylethyl)-3,7,17-trimethyl-13^1,15^1-cyclo-21H,23H-porphin (XVI). A mixture of complexes (XII)/(XIII) (150 mg) was thermolyzed under the conditions described above for complex (II). Complex (XIV) (10 mg), complex (XVI) (30 mg), and complex (XV) (5 mg) were isolated after chromatographic resolution on a column of silica gel in chloroform−acetone (95:5).

Complex (XIV). PMR spectrum: 9.76 and 9.75 (2H, 2H, two s, meso-H); 4.24 and 3.16 (two t, $C\underline{H}_2C\underline{H}_2CO$), 3.68 (s, 4 × $COOC\underline{H}_3$); 3.48 (s, CH_3-ring).

Complex (XV). PMR spectrum: 9.82, 9.79, 9.77 (all s, 20-H, 10-H, 5-H); 7.46 (d, 15^1-H); 5.18 (m, 13^1-H); 4.62 (m, 17^1-CH_2); 4.27-4.13 (m, $C\underline{H}_2CH_2CO$); 3.71 and 3.66 (3H, 6H, two s, 3 × $COOCH_3$); 3.53, 3.485, 3.47 (all s, 2-, 18-, 8-CH_3); 3.49 (d, J = 1.1 Hz, 12-CH_3); 3.41 and 3.26 (two d.d, 13^1-CH_2); 3.26-3.05 (m, 3 × $CH_2C\underline{H}_2CO$); 2.69 (s, N−CH_3).

Complex (XVI). PMR spectrum: 9.71, 9.65, 9.57 (all s, meso-H); 4.81 and 3.72 (2H, 2H, two m, CH_2CH_2-exocycle); 4.20-4.10 and 3.17-3.12 (two m, CH_2/CH_2CO); 3.75, 3.70, 3.68, 3.675 (all s, 4 × $COOCH_3$); 3.47, 3.44, 3.26 ppm (all s, 3 × CH_3-ring). Mass spectrum, m/e (%): 778 (M^+, 100), 705 (36).

Nickel Complexes of 3,8,18-Tri-(2-ethoxycarbonylethyl)-2,7,12,17-tetramethyl-13^1-carboxymethyl-15^1-(N-benzyl)amino-21H,23H-porphin Lactam (XXI) and 3,8,18-Tri-(2-ethoxycarbonylethyl)-2,7,12,17-tetramethyl-13^1-carboxymethyl-15^1-[N-(2-phenylethyl)]amino-21H,23H-porphin Lactam (XXII). The Schiff's bases (XIX) and (XX) were obtained in 75 and 70% yield from complex (I) and benzylamine or phenylethylamine as described above for complex (II).

Thermolysis of these gave complexes (XXI) and (XXII) in 2 and 15% yield, respectively. Treatment of complex (XXII) with concentrated H_2SO_4 gave porphyrin (XXIII) in 80% yield.

Complex (XIX). PMR spectrum: 10.82 (s, CH=N); 9.53 and 9.52 (two s, 1H, 2H, meso-H); 7.37 and 7.25 (two m, o-, m-, p-Ph protons); 5.19 (s, CH_2Ph); 4.21-3.98 (overlapping q and t, $C\underline{H}_2CH_3$, $C\underline{H}_2CH_2CO$); 3.41, 3.40, 3.39, 3.09 (all s, CH_3-ring); 3.08, 3.0, 2.89 (all t, $CH_2C\underline{H}_2CO$); 1.27, 1.20, 1.18, and 1.17 ppm (all t, 4 × $CH_2C\underline{H}_3$).

Complex (XX). PMR spectrum: 10.69 (s, CH=N−); 9.533, 9.528 (1H, 2H, two s, meso-H); 7.22, 7.15 (two m, o-, m-, p-Ph protons); 4.23-4.11 (4 × $C\underline{H}_2CH_3$, $C\underline{H}_2CH_2Ph$, 3 × $C\underline{H}CH_2CO$); 3.87 and 2.89 (two m, $CH_2C\underline{H}CO$); 3.42, 3.41, 3.37, 2.99 (all s, CH_3-ring); 1.27, 1.22, 1.19, 1.18 ppm (all t, $CH_2C\underline{H}_3$).

Complex (XXI). PMR spectrum: 9.78, 9.75 (2H, 1H, meso-H); 7.54 (H_x, d, J = 5.4 Hz); 7.18, 7.08, 6.96 (t, t, d, m-, p-, o-Ph protons); 5.23 (m, H_y); 4.36 and 3.58 (two d, J = 14.5 Hz, CH_2Ph); 4.27-4.12 (m, $C\underline{H}_2CH_2CO$, $C\underline{H}_2CH_3$); 3.50, 3.49 (two s, 6H, 3H, 3 × CH_3-ring); 2.99 (s, 17-CH_3); 3.59 (H_a, d.d, J_{ay} = 9.9 Hz, J_{ab} = 17 Hz); 3.38 (H_b, d.d, J_{ab} = 17 Hz, J_{by} = 2.2 Hz); 3.15, 3.14, 3.04 (all t, $CH_2C\underline{H}_2CO$); 1.19, 1.18, 1.17 ppm (all t, 3 × $CH_2C\underline{H}_3$).

Complex (XXII). PMR spectrum: 9.72, 9.70 (2H, 1H, two s, meso-H); 7.41 (H_x, d, J = 5.4 Hz); 6.75, 6.70, 6.29 (t, t, d, m-, p-, o-Ph Protons); 5.01 (H_y, m); 4.22-4.13 ($C\underline{H}_2CH_2CO$, $C\underline{H}_2CH_3$); 3.48, 3.47, 3.45 (all s, 3H, 3H, 6H, CH_3-ring); 3.39 (H_a, d.d, J_{ay} = 9.9 Hz, J_{ab} = 17 Hz); 3.24 (H_b, d.d, J_{ab} = 17 Hz, J_{by} = 2.0 Hz); 3.48 and 3.17 (two m, $C\underline{H}_2CH_2Ph$); 3.13-3.02 ($CH_2C\underline{H}_2CO$); 2.28 and 1.30 (two m, $CH_2C\underline{H}_2Ph$); 1.21, 1.19, 1.17 ppm (all t, 3 × $CH_2C\underline{H}_3$).

Porphyrin (XXIII). PMR spectrum: 10.17, 10.12, 10.06 (all s, 20-, 5-, 10-H); 7.72 (H_x, d, J = 5.4 Hz); 6.64, 6.54, 6.15 (t, t, d, m-, p-, o-Ph protons); 5.14 (H_y, m); 4.46, 4.46, 4.35 (overlapping t, 8^1-, 18^1-, 3^1-CH_2); 4.19-4.16 (m, 3 × $C\underline{H}_2CH_3$); 3.75, 3.72, 3.619, 3.616 (all s, 17-, 7-, 12-, 2-CH_3); 3.55, 3.49 (two m, 13^1-CH_2); 3.28-3.22 (m, $CH_2C\underline{H}_2CO$); 3.70 and 3.42 (two m, $C\underline{H}_2CH_2Ph$); 2.25 and 1.05 (two m, $CH_2C\underline{H}_2Ph$); 1.20, 1.19, 1.17 (all t, 3 × $CH_2C\underline{H}_3$); −2.90, −3.83 ppm (two s, NH).

3,8,18-Tri-(carboxyethyl)-2,7,12,17-tetramethyl-13^1,15^1-cyclo-13^1-carboxymethyl-15^1-N-methyl)amino-21H,23H-porphin Lactam Dihydrochloride (XXIV). The porphyrin (IX) (200 mg) was kept in a mixture of concentrated HCl (10 ml) and water (20 ml) for 1 week in the refrigerator. The precipitated crystals were filtered off and the porphyrin (XXIV) (176 mg: 89%) was obtained. PMR spectrum in $CDCl_3$ + 10% CF_3COOD: 10.94, 10.93, 10.83 (all s, meso-H); 7.97 (H_x, d, J = 5.5 Hz); 5.7 (m, H_y); 4.52 (m, 3 × $C\underline{H}_2CH_2CO$); 3.87 (H_a, d.d, J_{ay} = 9.9 Hz, J_{ab} = 17 Hz); 3.82, 3.75, 3.73 (all s, CH_3-ring); 3.42 (H_b, d.d); 3.40-3.30 (3 × $CH_2C\underline{H}_2CO$); 3.24 ppm (s, N−CH_3).

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