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PORPHYRINS. 37.* SYNTHESIS OF HETERODIMERS OF PORPHYRINS AND CHLORINS CONTAINING PYRROLYL-METHYL BRIDGES*[2]

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We have obtained various adducts, including homodimers and heterodimers of ethanebisporphyrins and ethanebischlorins containing pyrrole and dipyrrylmethane insertions, by reaction of meso-dimethylaminomethylporphyrins and chlorins with α-unsubstituted pyrrole derivatives in the presence of methyl iodide.

Keywords: bisporphyrinylmethylpyrroles, heterodimers, *meso*-dimethylaminomethylporphyrins, *meso*-dimethylaminomethylchlorins, pyrrolylmethylporphyrins.

During a targeted study in the area of the chemistry of mesoporphyrinylmethyl cations, we recently observed a novel reaction of *meso*-dimethylaminomethyl(DMAM)porphyrins **1-3** (through formation of the corresponding methoiodides of DMAM-porphyrins **4-6**) with α-unsubstituted pyrroles **7-9** [2,3]. We obtained various adducts **10-15** (Scheme 1).

Using α, α'-unsubstituted pyrroles as the pyrrole component makes it possible to obtain either symmetric diporphyrinylmethylpyrrole adducts of type **16** (treatment with an excess of the methoiodide of DMAM-porphyrin) (Scheme 2), or porphyrinylmethylpyrroles **10, 11, 14, 15**, containing an α-unsubstituted pyrrole moiety (treatment with excess pyrrole) (Scheme 1).

Reaction of porphyrinylmethylpyrrole **14** with methoiodides of DMAM derivatives of porphyrin **3** and chlorin **17** [4] led to formation of asymmetric adducts: the heterodimers **18** and **19** (Scheme 3).

Furthermore, as the pyrrole component we can use the dipyrrolylmethane derivative **20**, which when reacting with excess methoiodides **4** or **6** gives the symmetric adducts **21** or **22**: porphyrin dimers linked by a dipyrrylmethane bridge (Scheme 4).

The reaction of excess dipyrrylmethane **20** with the methoiodide of DMAM-porphyrin (for example, **1**) led to formation of the hypothetical monoadduct **23** (scheme 5), but we could not isolate the latter due to the similarity of its chromatographic mobility to the mobility of the starting dipyrrylmethane **20**.

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* For Communication 36, see [1].

*[2] Dedicated to Professor M. A. Yurovskaya on her Jubilee.

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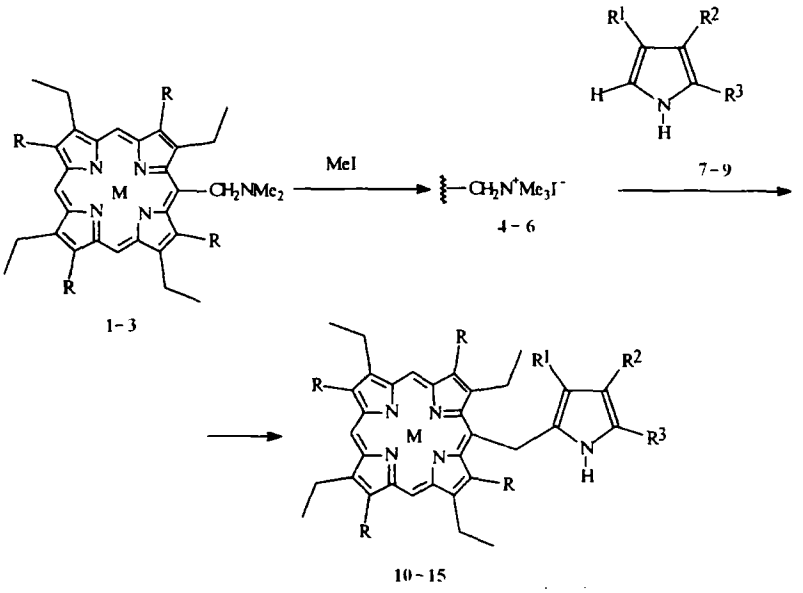
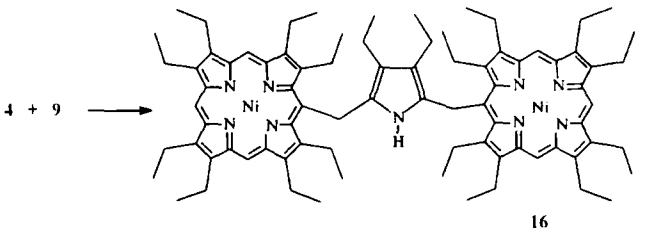
Scheme 1



1, 4 R = Et, M = Ni; **2, 5** R = Me, M = Ni; **3, 6** R = Me, M = 2H; **7** $R^1 = R^2 = R^3 = H$; **8** $R^1 = R^3 = Me$, $R^2 = COOEt$; **9** $R^1 = R^2 = Et$, $R^3 = H$; **10** R = Me, M = Ni, $R^1 = R^2 = R^3 = H$; **11** R = Me, M = 2H, $R^1 = R^2 = R^3 = H$; **12** R = Me, M = Ni, $R^1 = R^3 = Me$, $R^2 = COOEt$; **13** R = Me, M = 2H, $R^1 = R^3 = Me$, $R^2 = COOEt$; **14** R = Et, M = Ni, $R^1 = R^2 = Et$, $R^3 = H$; **15** R = Me, M = 2H, $R^1 = R^2 = Et$, $R^3 = H$

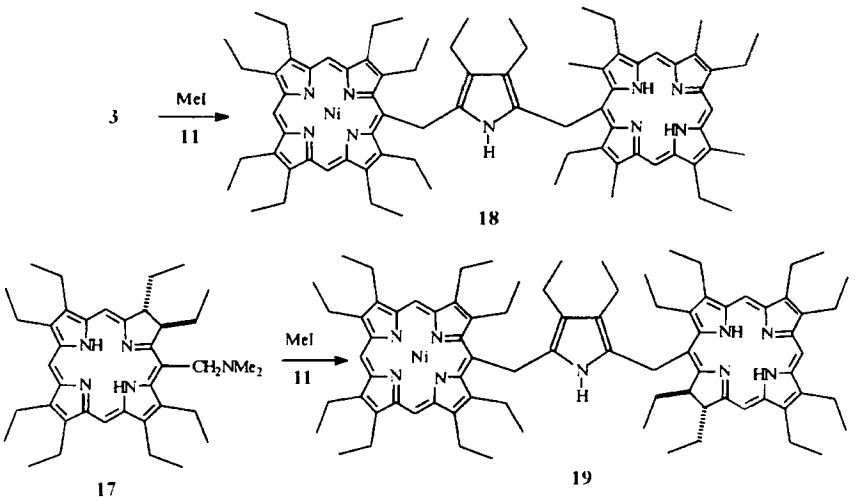
Scheme 2



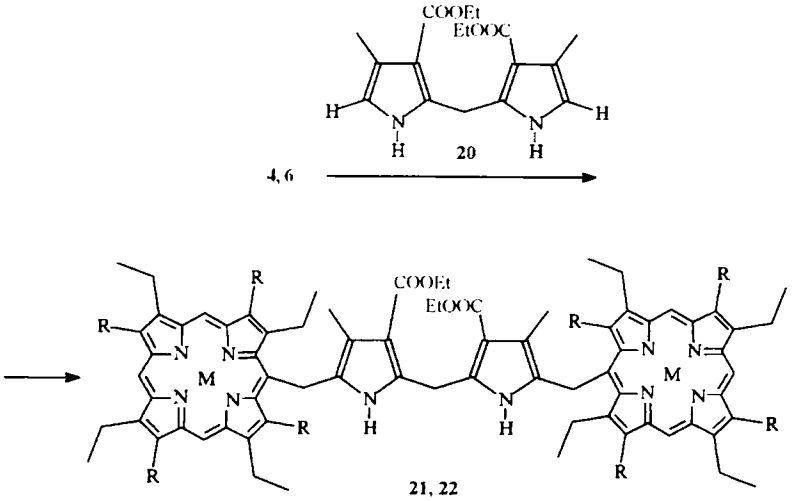
Using a nickel complex of the tetramethyl ester of coproporphyrin I **24** [5] as the porphyrin component of the DMAM derivative made it possible to avoid the complications of isolating monoadduct **25** (Scheme 6). The derivative obtained by reacting with excess porphyrin **26** in the presence of methyl iodide gives the porphyrin heterodimer with dipyrrylmethane insertion **27** in high yield.

Investigation of the structure of the adducts obtained containing the dipyrrylmethane moiety (compounds **21**, **22**, and **27**) by ^1H NMR in $CDCl_3$ solution showed that their conformation is unusual, which was apparent in the upfield shift of the signals from the ethyl moiety of the ethoxycarbonyl of the pyrrole part. So this signal from the methyl groups was observed at 0.91 and 0.66 ppm for compounds **21** and **22** respectively, while in the "monomeric" adducts **12** and **13**, its position was normal -1.37 ppm. The signal from the protons in the CH_2 groups

Scheme 3

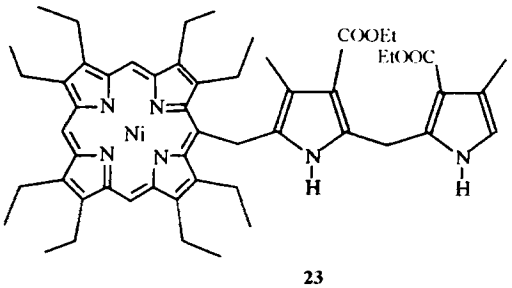


Scheme 4

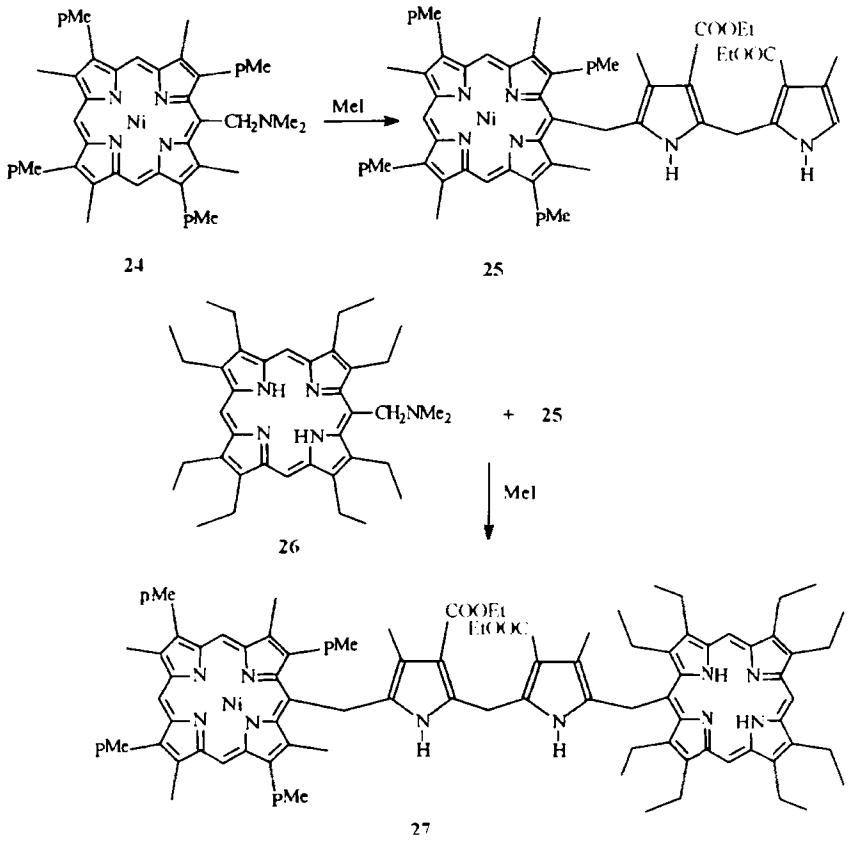


21 R = Et, M = Ni; **22** R = Me, M = 2H

Scheme 5



Scheme 6



R = CH_2CH_2COOMe

was shifted even more: this signal was now found at 1.20 and 1.65 ppm for **22** and **21** respectively, in contrast to 4.30 ppm for compounds **12** and **13**.* The ^1H NMR spectrum of the heterodimer **27** is a peculiar type of "mixture" of the spectra of the homodimers **21** and **22**, in which the signals from the methyl group of the ethyl ester appear at -0.53 ppm and -1.01 ppm (the signals from the methylene groups of the ethyl esters lie in the region overlapping the signals from the methyl groups of octaethylporphyrin). These data are probably evidence that the porphyrin-dipyrrylmethane-porphyrin chain is folded, and the carbethoxyl groups in the β-positions of the pyrroles are located in a zone where they are shielded by the ring currents of the porphyrins.

EXPERIMENTAL

The ^1H NMR spectra were obtained on Bruker WM-360 and Varian UNITY-300 instruments in $CDCl_3$, internal standard TMS or the $CHCl_3$ signal at 7.27 ppm; the electronic spectra were obtained on Hitachi-320 and Varian Cary 3 spectrophotometers. The mass spectra of the dimers were obtained on a Finnigan MAT 90 [7]. For chromatographic separation of the compounds, we used Merck silica gel (G 60, 0.040-0.063 mm) for column chromatography.

* The signals from the CH_2 and CH_3 groups for compound **20** [6] appear as a quadruplet at 4.30 ppm and 1.38 ppm respectively.

General Procedure for Obtaining Adducts 10-15 and 25. A solution of the DMAM derivative of porphyrin **1-3, 24** (~10 mg/ml), methyl iodide (10 equivalents), and the corresponding pyrrole **7-10, 20** (3-5 equivalents) in methylene chloride was held at 40°C for 1-2 h. The compounds **10-15, 25** obtained were purified by chromatography on silica gel.

Compound 10. Yield 89%, starting from compounds **2** and **7**. ^{1}H NMR spectrum: 9.45 and 9.44 (1H and 2H, both s, *meso*-H); 6.55 (1H, br. s, NH-pyrrole); 6.05-5.90 (5H, m, PorC$\underline{H}_2$Pyr and 3 × H-pyrrole); 3.95-3.75 (8H, m, PorC$\underline{H}_2$CH$_3$); 3.39 , 3.38 , 3.35 , and 3.34 (12H, all s, PorC$\underline{H}_3$); 1.76, 1.75, 1.70, and 1.67 ppm (12H, all t, J = 7.5 Hz, PorCH$_2$C$\underline{H}_3$); UV spectrum: λ_{max} (relative intensity): 406 (10.0), 530 (1.0), 564 nm (1.4); mass spectrum, *m/z* (relative intensity, %): 613 (M$^+$, 52), 548 (2), 534 (100).

Compound 11. Yield 82%, starting from compounds **3** and **7**. ^{1}H NMR spectrum: 10.15 and 9.90 (2H and 1H, two s, *meso*-H); 7.51 (1H, br. s, NH-pyrrole); 6.40 and 6.25 (5H, m, PorC$\underline{H}_2$Pyr and 3 × H-pyrrole); 4.20-3.95 (8H, m, PorC$\underline{H}_2$CH$_3$); 3.66, 3.65, 3.59, and 3.37 (12H, all s, PorC$\underline{H}_3$); 1.88, 1.82, and 1.73 (3H, 6H, and 3H, all t, J = 7.5 Hz, PorCH$_2$C$\underline{H}_3$) -2.80 ppm (2H, br. s, NH-porphyrin); UV spectrum: λ_{max} (relative intensity): 408 (6.7), 504 (1.0), 540 (0.7), 572 (0.6), 624 (0.4) nm; mass spectrum, *m/z*: (relative intensity, %): 557 (M$^+$, 100), 492 (10).

Compound 12. Yield 89%, starting from compounds **2** and **7**. ^{1}H NMR spectrum: 9.49 and 9.48 (1H and 2H, both s, *meso*-H); 6.64 (1H, br. s, NH-pyrrole); 5.70 (2H, br. s, PorC$\underline{H}_2$Pyr); 4.30 (2H, q, J = 7.5 Hz, OC$\underline{H}_2$CH$_3$); 3.95-3.65 (8H, m, PorC$\underline{H}_2$CH$_3$); 3.40, 3.41, 3.37, and 3.22 (12H, all s, PorC$\underline{H}_3$); 2.56 and 1.93 (3H and 3H, two s, CH$_3$-pyrrole); 1.78, 1.70, and 1.63 (3H, 6H, and 3H, all t, J = 7.5 Hz, PorCH$_2$C$\underline{H}_3$); 1.38 ppm (3H, t, J = 7.5 Hz, OCH$_2$C$\underline{H}_3$); UV spectrum: λ_{max} (relative intensity):404 (10.0), 524 (1.0), 560 nm (1.3); mass spectrum, *m/z* (relative intensity, %): 713 (M$^+$, 100), 548 (26).

Compound 13. Yield 94%, starting from compounds **3** and **8**. ^{1}H NMR spectrum: 10.19 and 9.94 (2H and 1H, both s, *meso*-H); 7.10 (1H, br. s, NH-pyrrole); 6.22 (2H, m, PorC$\underline{H}_2$Pyr); 4.30 (2H, q, J = 7.5 Hz, OC$\underline{H}_2$CH$_3$); 4.10 (8H, m, PorC$\underline{H}_2$CH$_3$); 3.64, 3.63, 3.61, and 3.34 (12H, all s, PorC$\underline{H}_3$); 2.70 and 1.90 (3H and 3H, s, CH × 3-pyrrole); 1.75 (12H, m, PorCH$_2$C$\underline{H}_3$); 1.36 (3H, t, J = 7.5 Hz, OCH$_2$C$\underline{H}_3$); -2.95 and -3.15 ppm (1H and 1H, br. s, NH-porphyrin); UV spectrum: λ_{max} (relative intensity): 406 (7.1), 504 (1.0), 540 (0.6), 575 (0.5), 624 (0.4) nm; mass spectrum, *m/z* (relative intensity, %): 657 (M$^+$, 100), 492 (6).

Compound 14. Yield 94%, starting from compounds **1** and **9**. ^{1}H NMR spectrum: 9.42 and 9.40 (1H and 2H, both s, *meso*-H); 5.80 (2H, s, PorC$\underline{H}_2$Pyr); 5.74 (1H, br. s, NH-pyrrole); 5.63 (1H, d, J = 2.4 Hz, α-H pyrrole); 3.88-3.67 (16H, overlapping q, CH$_2$ of ring CH$_2$CH$_3$); 2.67 and 2.32 (4H, q, J = 7.5 Hz, PyrC$\underline{H}_2$CH$_3$); 1.80-1.63 (24H, overlapping t, CH$_3$ of ring CH$_2$C$\underline{H}_3$); 1.28 and 1.00 ppm (6H, t, J = 7.5 Hz, PyrCH$_2$C$\underline{H}_3$); UV spectrum: λ_{max} (relative intensity): 408 (17.9), 532 (1.0), 565 nm (1.53); mass spectrum, *m/z* (relative intensity, %): 726 (M$^+$, 65), 604 (PorCH$_2^+$, 35).

Compound 15. Yield 80%, starting from compounds **3** and **9**. ^{1}H NMR spectrum: 10.15, 10.13, and 9.91 (3H, all s, *meso*-H); 6.90 (1H, br. s, NH-pyrrole); 6.24 and 6.20 (2H, AB, J_{gem} = 15 Hz, PorC$\underline{H}_2$Pyr); 6.09 (1H, s, α-H-pyrrole); 4.15-3.95 (8H, overlapping q, CH$_2$ of ring CH$_2$CH$_3$); 3.65, 3.63, 3.59, and 3.31 (12H, all s, PorCH$_3$); 2.94 and 2.63 (4H, two q, J = 7.5 Hz, PyrC$\underline{H}_2$CH$_3$); 1.90-1.70 (12H, overlapping t, CH$_3$ of ring CH$_2$CH$_3$); 1.53 and 1.25 (6H, two t, J = 7.5 Hz, PyrCH$_2$C$\underline{H}_3$); -3.00 ppm (2H, br. s, NH-porphyrin); UV spectrum: λ_{max} (relative intensity): 405 (66.5), 505 (5.6), 539 (2.6), 574 (2.3), 623 nm (1.0).

Compound 25. Obtained in 86% yield, starting from **24** [5] and **20**, and used for synthesis of compound **27**, which was characterized.

General Procedure for Obtaining Adducts 16, 18, 19, 21, 22, 27. A solution of the DMAM derivative of porphyrin **(1, 3, 17, 26)** (1.5 equivalents) (~10 mg/ml), methyl iodide (10 equivalents), and the corresponding pyrrole (or porphyrinylmethylpyrrole) **(9, 14, 20, 25)** in methylene chloride was held at 40°C for 1-2 h. The compounds obtained **16, 17, 19, 21, 22, 27** were purified by chromatography on silica gel.

Compound 16. Obtained in 75% yield, starting from compounds **1** and **9**. ^{1}H NMR spectrum: 9.29 and 8.58 (2H and 4H, both s, *meso*-H); 6.73 (1H, br. s, NH-pyrrole); 5.20 (2H, s, PorC$\underline{H}_2$Pyr); 3.80-2.60 (32H, overlapping q, CH$_2$ of ring CH$_2$CH$_3$); 2.32 (4H, q, J = 7.5 Hz, PyrC$\underline{H}_2$CH$_3$); 1.80-1.10 (48H, overlapping t, CH$_3$ of ring CH$_2$CH$_3$); 0.93 ppm (6H, t, J = 7.5 Hz, PyrCH$_2$C$\underline{H}_3$); UV spectrum: λ_{max} (relative intensity): 402 (11.1), 532 (1.0), 565 nm (1.38).

Compound 18. Obtained in 71% yield, starting from **3** and **14**. UV spectrum: λ_{max} (relative intensity): 401 (33.3), 508 (2.7), 537 (2.8), 572 (2.4), 627 (1.0) nm.

Compound 19. Obtained in 81% yield, starting from compounds **17** [4] and **11**. ^{1}H NMR spectrum: 9.62, 9.22, 8.94, 8.78, and 8.12 (1H, 1H, 1H, 1H, and 2H, s, *meso*-H of porphyrin and chlorin); 6.68 (1H, br. s, NH-pyrrole); 5.17 (2H, s, PorC$\underline{H}_2$Pyr); 5.22 and 5.06 (2H, AB, J_{gem} = 17 Hz, ChlC$\underline{H}_2$Pyr); 4.10-0.20 (82H, overlapping q, t, and m, CH_2 of ring CH_2CH_3, CH_3 of ring CH_2CH_3, PyrCH$_2$C$\underline{H}_3$, PyrCH$_2$C$\underline{H}_3$); -1.68 and -2.40 ppm (2H, br. s, NH-chlorin); UV spectrum: λ_{max} (relative intensity): 399 (23.5), 503 (1.8), 532 (1.4), 566 (1.7), 591 shoulder (1.0), 653 nm (4.9).

Compound 20. Obtained as in [6]. ^{1}H NMR spectrum: 9.40 (2H, br. s, NH); 6.32 (2H, br. s, α-H-pyrrole); 4.42 (2H, s, PyrCH$_2$Pyr); 4.30 (4H, q, J = 7.5 Hz, OC$\underline{H}_2$CH$_3$); 2.15 (6H, s, CH_3-pyrrole); 1.38 ppm (6H, t, J = 7.5 Hz, OCH$_2$C$\underline{H}_3$).

Compound 21. Obtained in 70% yield, starting from compounds **1** and **20**. ^{1}H NMR spectrum: 9.47 and 9.46 (4H and 2H, both s, *meso*-H); 8.38 (2H, s, NH-pyrrole); 5.52 (4H, s, PorC$\underline{H}_2$Pyr); 3.90-3.40 (32H, m, PorC$\underline{H}_2$CH$_3$); 3.57 (2H, s, PyrC$\underline{H}_2$Pyr); 2.37 (6H, s, CH_3-pyrrole); 1.90-1.50 (52H, m, OC$\underline{H}_2$CH$_3$ and PorCH$_2$C$\underline{H}_3$); -0.66 ppm (6H, t, J = 7.5 Hz , OCH$_2$C$\underline{H}_3$); UV spectrum: λ_{max} (relative intensity): 407 (14.8), 529 (1.0), 564 nm (1.5).

Compound 22. Obtained in 70% yield, starting from compounds **3** and **20**. ^{1}H NMR spectrum: 10.16 and 9.92 (4H and 2H, both s, *meso*-H); 8.60 (2H, br. s, NH-pyrrole); 6.03 (4H, br. s , PorC$\underline{H}_2$Pyr); 4.20-3.95 (16H, m, PorC$\underline{H}_2$CH$_3$); 3.65, 3.62, 3.56, and 3.11 (24H, s, PorC$\underline{H}_3$); 3.44 (2H, s, PyrC$\underline{H}_2$Pyr); 2.47 (6H, s, CH_3-pyrrole); 1.90-1.55 (24H, m, PorCH$_2$C$\underline{H}_3$); 1.10 (4H, q, J = 7.5 Hz, OC$\underline{H}_2$CH$_3$); -0.91 (6H, t, J = 7.5 Hz, OCH$_2$C$\underline{H}_3$); -3.00 ppm (4H, br. s, NH-porphyrin); UV spectrum: λ_{max} (relative intensity): 404 (30.5), 505 (3.9), 537 (2.5), 574 (1.9), 627 nm (1.0).

Compound 27. Obtained in 98% yield, starting from compounds **26** and **25**. ^{1}H NMR spectrum: 10.14 and 9.90 (2H and 1H, both s, *meso*-H-octaethylporphyrin); 9.49 and 9.46 (1H and 2H, both s, *meso*-H-coproporphyrin); 8.55 and 8.60 (2H, br. s, NH-pyrrole) 6.15 and 5.40 (4H, br. s, PorC$\underline{H}_2$Pyr); 4.20-3.95 (24H, m, PorC$\underline{H}_2$CH$_2$COOCH$_3$ and PorC$\underline{H}_2$CH$_3$); 3.73 and 3.72 (12H, s, PorCH$_2$CH$_2$COOC$\underline{H}_3$); 3.58, 3.44, 3.42, and 3.34 (12H, s, PorC$\underline{H}_3$); 3.20-3.00 (8H, m, PorCH$_2$C$\underline{H}_2$COOCH$_3$); 2.96 (2H, s, PyrC$\underline{H}_2$Pyr); 2.56 and 2.15 (6H, s, CH_3-pyrrole); 2.00-1.40 (28H, m, PorCH$_2$C$\underline{H}_3$ and OC$\underline{H}_2$CH$_3$); -0.53 and -1.01 (6H, t, J = 7.5 Hz, OCH$_2$C$\underline{H}_3$); -2.80 ppm (2H, br. s, NH-octaethylporphyrin); UV spectrum: λ_{max} (relative intensity): 405 (93), 424 (71), 501 (6), 528 (7), 560 (11), 622 nm (1.0).

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REFERENCES

1. G. V. Ponomarev, D. V. Yashunsky, V. V. Borovkov, E. Sakata, and D. P. Arnold, *Khim. Geterotsikl. Soedin.*, No. 12, 1627 (1997).
2. D. V. Yashunsky, A. S. Moskovkin, and G. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, No. 1, 136 (1996).
3. D. V. Yashunsky, G. V. Ponomarev, and D. P. Arnold, *Tetrahedron Letters*, **38**, 105 (1997).
4. G. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, No. 12, 1694 (1993).
5. M. O. Senge, G. V. Ponomarev, T. P. Forsyth, and K. M. Smith, *Z. Naturforsch.*, **51B**, 1644 (1996).
6. H. Fischer and P. Halbig, *Ann.*, **447**, 135 (1926).
7. I. M. Karnaukh, A. S. Moskovkin, and G. V. Ponomarev, *Khim. Geterotsikl. Soedinen.*, No. 11, 1478 (1993).