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PORPHYRINS. 38*. REACTION OF PORPHYRINS CONTAINING HYDROXY-(ALKOXY)ETHYL OR ALKOXYMETHYL SUBSTITUENTS WITH NUCLEOPHILES IN THE PRESENCE OF ZINC ACETATE. A NOVEL, PROMISING METHOD FOR THE MODIFICATION OF PORPHYRINS ON THE PERIPHERY OF THE MACROCYCLE

G. V. Ponomarev[1], G. V. Kirillova[2], and D. V. Yashunsky[1]

Porphyrins which contain 1-hydroxy(alkoxy)ethyl or alkoxymethyl substituents on the periphery of the macrocycle (i.e. formally able to yield "benzyl type" carbocations) react with nucleophiles (4-tert-butylphenol or the β-diketones acetylacetone, benzoylacetone, dibenzoylmethane, or 4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione) in the presence of excess zinc acetate. They give high yields of the corresponding addition products, which are the zinc complexes of porphyrins with a 1-(4-tert-butylphenoxy)ethyl substituent or with substituents containing β-diketone residues.

Keywords: zinc acetate, deuteroporphyrin, 2,4-dialkoxymethylporphyrins, β-diketones.

It is known that a whole series of porphyrins and chlorins have the ability to accumulate selectively in tumor tissues and this property is used in medicinal practice for photodynamic therapy in cancer. One novel approach in the search for novel photosensitizers for photodynamic therapy is based on natural porphyrins and chlorins with the introduction of various substituents in positions 2 and 4 of deuteroporphyrin-IX **1** or modification of the vinyl group in derivatives of chlorophyll-a. It was found that exchange of hydroxyl groups in the hematoporphyrin-IX **2** for alkoxyl can markedly affect the tropism of the corresponding photosensitizers to tumors. In addition the relationship between the size and degree of branching of the alkoxy radical and the photodynamic activity of the corresponding porphyrin during *in vivo* experiments was followed (for details see review [3]).

The preparation of porphyrins which have different alkoxy substituents in place of hydroxy groups in porphyrin **2** most frequently involves a variation of the original preparation of "perbromide" **3** *via* solution of the natural protohemin-IX **4** or porphyrin **2** in a mixture of HBr and AcOH with subsequent treatment with the corresponding alcohol [4], amine [5], or thiol [6] according to Scheme 1.

However, this method has several limitations. Thus, treatment of the intermediate perbromide **3** with phenols gives the corresponding α-phenoxyethylporphyrins in only insignificant yield and is accompanied by formation of bromination products and reaction with CH-acids leads to a multitude of compounds of unknown structure.

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[1] Institute of Biomedical Chemistry, Russian Academy of Medical Sciences, 119832 Moscow, Russia; e-mail: gelii@medic.ibmh.msk.su. [2] Science and Manufacture Center "Pharmaprotection", 141400 Khimki, Russia.
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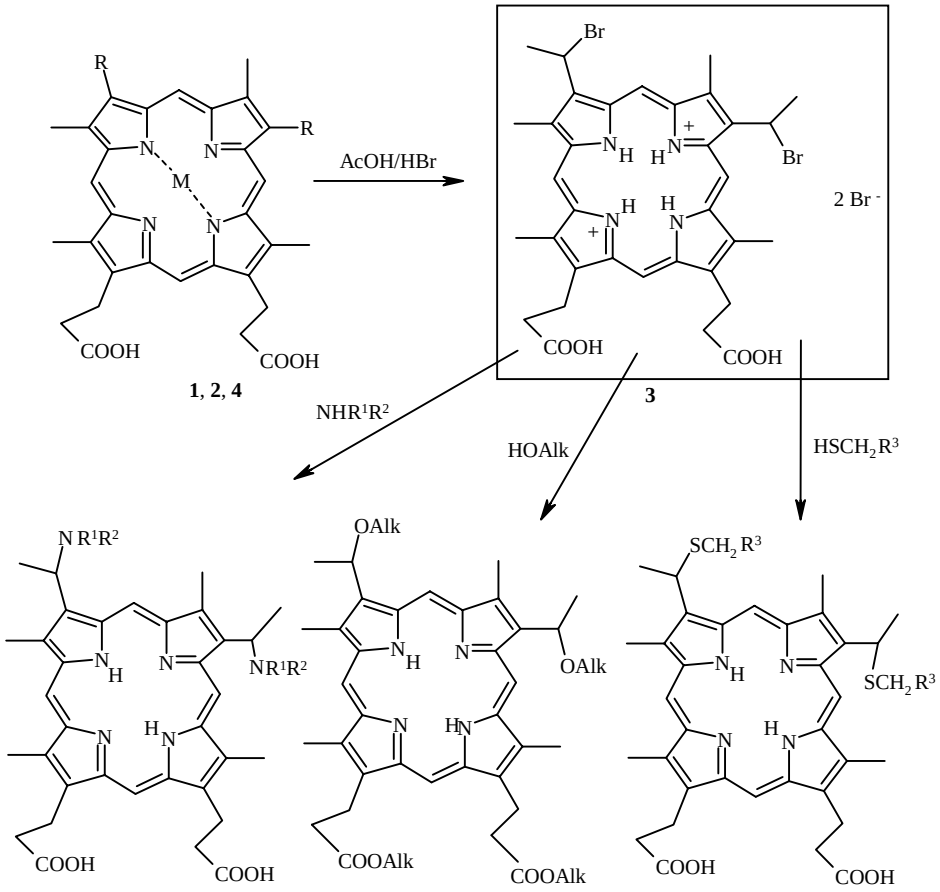
Scheme 1



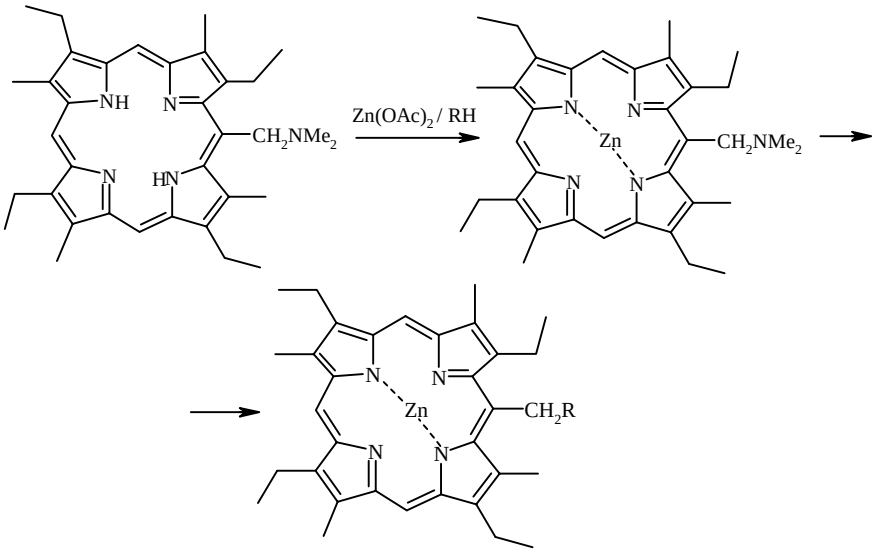
1 R = H, M = 2H; **2** R = CH(OH)Me, M = 2H;
4 R = CH=CH_2, M = Fe(III)Cl; R^1, R^2 = Me_2, Et_2, Im; R^3 = COOEt

During an investigation of the chemical properties of porphyrins containing a *meso*-dimethylaminomethyl (DMAM) group we have found that such compounds react readily with various nucleophiles (alcohols and CH-acids) in the presence of excess zinc acetate. This is used in the generation of the carbocation of the zinc complex of *meso*-methyleneporphyrin and forms the corresponding addition products together with dimethylamine [7-10] according to Scheme 2 (for details see review [11]):

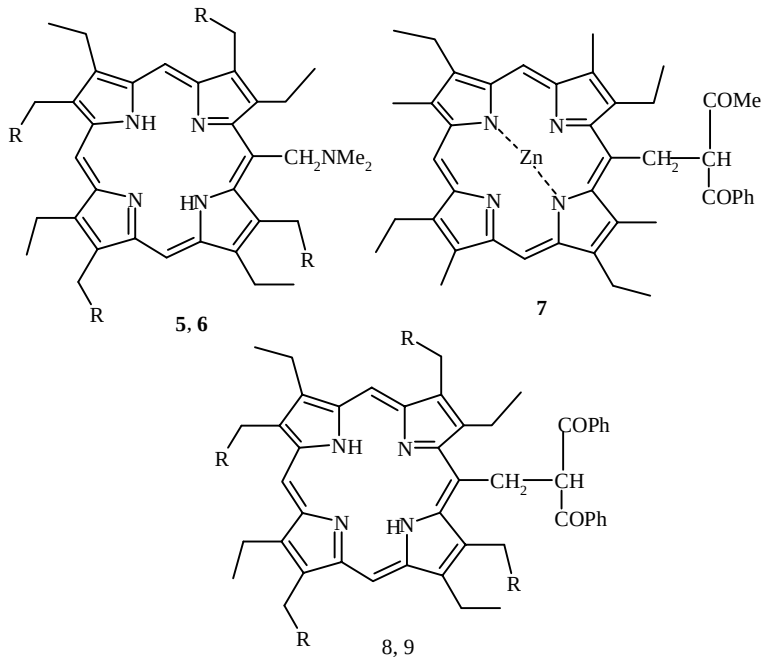
The reaction with acetylacetone occurs particularly readily [9]. We have shown that with other β-diketones, even those as bulky as benzoylacetone or dibenzoylmethane, the yield of the corresponding addition products reached 80-90%. Hence, heating *meso*-DMAM-etioporphyrin-I (**5**) and *meso*-DMAM-octaethylporphyrin (**6**) with benzoylacetone or dibenzoylmethane in carbon tetrachloride in the presence of zinc acetate gave the corresponding zinc complexes in 80-90% yield. Treatment of these for a short period with hydrochloric acid gave the corresponding porphyrin free bases. As an example, we give the ^{1}H NMR spectral data for compounds **7-9**. Introduction of butyl substituents into the porphyrin molecule has virtually no effect on the electronic spectrum in the visible region (400-600 nm) but the presence of aromatic phenyl rings is unambiguously detected in the UV part of the spectral region by the appearance of band in the region 240-260 nm.

However, DMAM groups on the peripheral (i.e. joined to the pyrrole rings) β-positions of the porphyrin ring [12] do not react directly with the corresponding nucleophiles in the presence of zinc acetate. With MeI and EtI respectively they form quite stable iodoalkylates [12, 13] which are converted to the iodomethylporphyrins upon refluxing with MeI. Only the latter give the corresponding alkoxymethylporphyrins [12] when heated with

Scheme 2



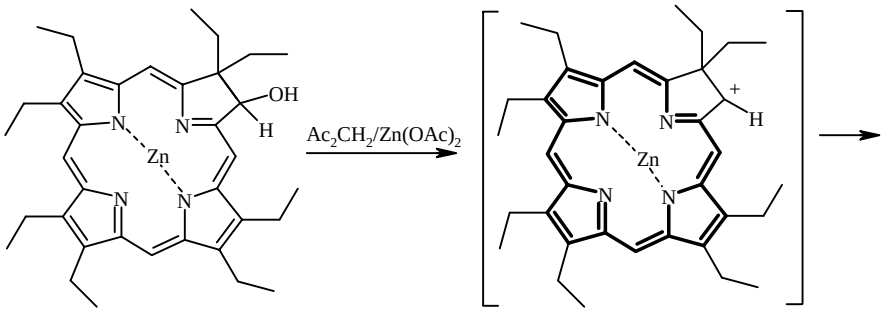
R = OAlk or OAr, CH_2NO_2, CH_2Ac, CH(CN)COOEt, $CH(NO_2)COOEt$, $CHAc_2$



6, **9** R = H; **5**, **8** R = Me

alcohols in the presence of zinc acetate. As the same time, β-hydroxychlorins are able to form the unusual "benzyl" carbocations in the presence of zinc acetate and to react with nucleophiles [14, 15]. Scheme 3 shows how the octaethylhydroxychlorin **10** (prepared by reduction of the corresponding octaethylporphyrin ketone with sodium borohydride) forms an adduct with acetyl acetone **11** when heated in acetonitrile in the presence of zinc acetate. In our opinion, the intermediate may be a zinc complex, the aromatic part of the molecule being shown by heavy lines in scheme:

Scheme 3



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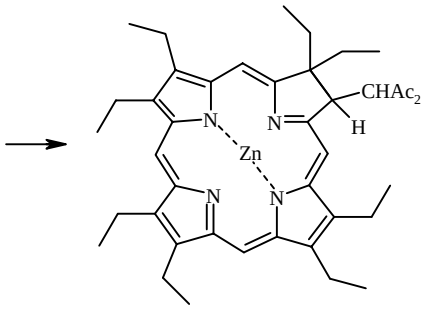

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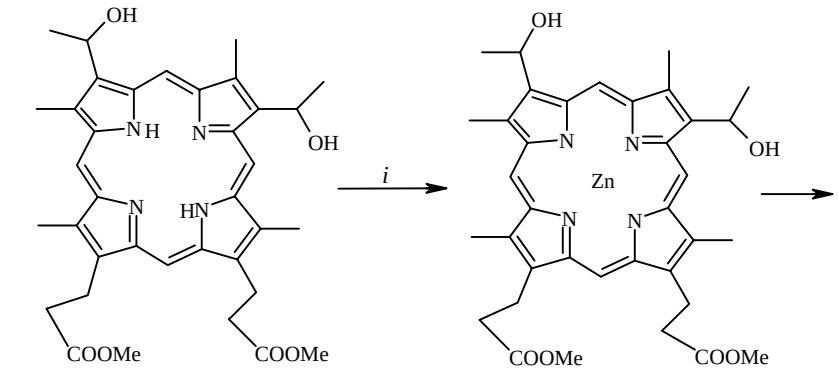
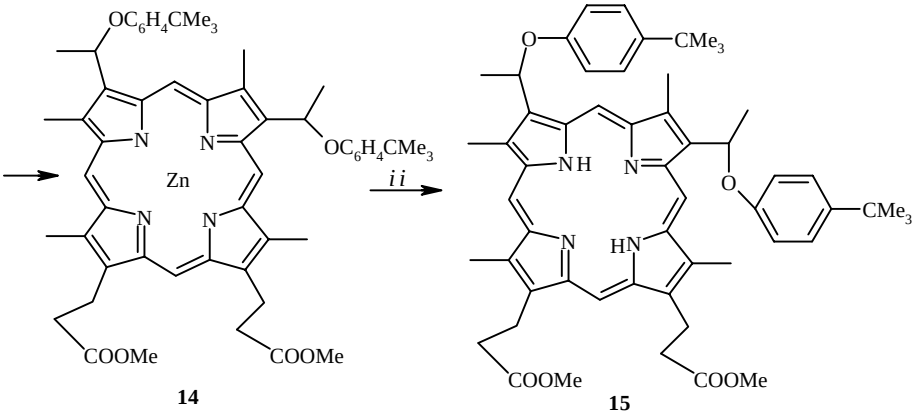
Scheme 4



12 **13**



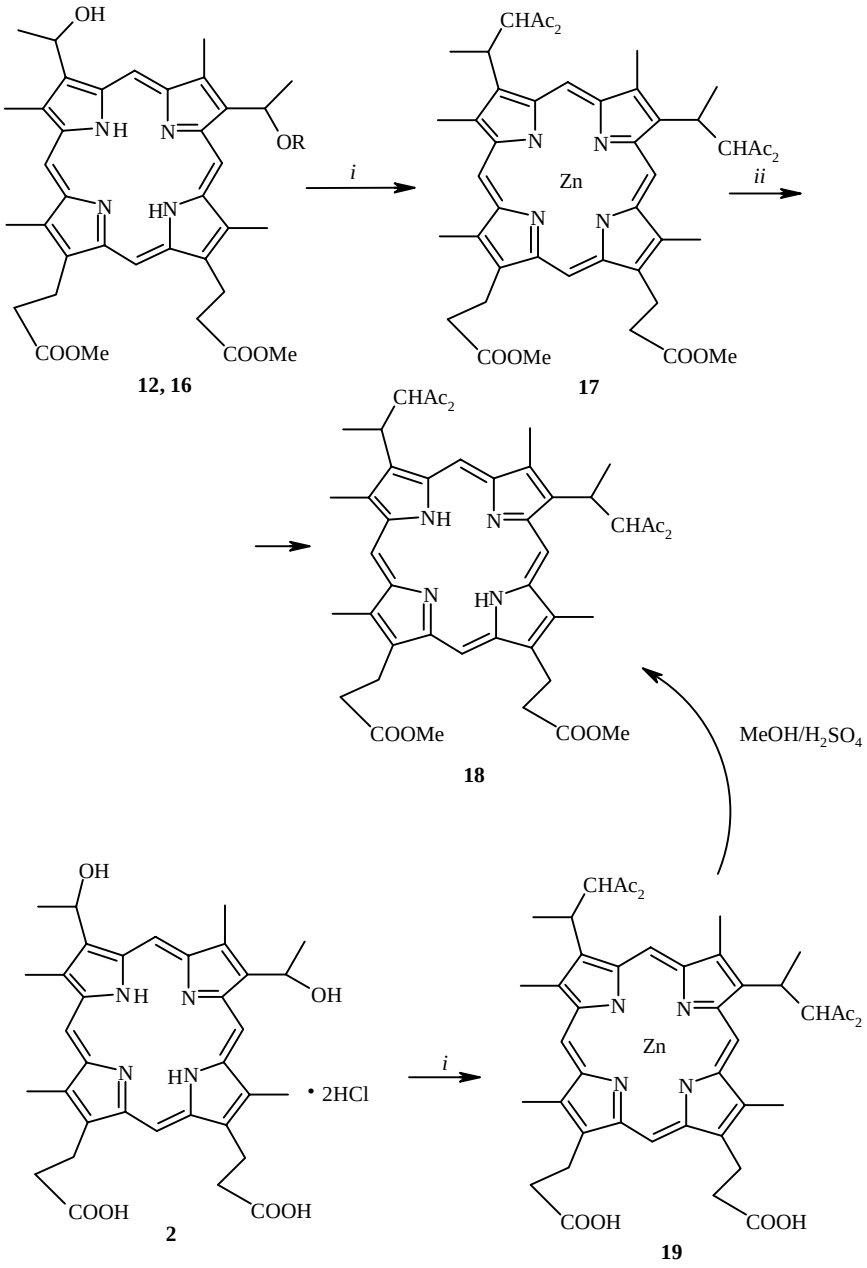
14 **15**

i $Zn(OAc)_2$, $HOC_6H_4CMe_3$-*p*/CCl_4–$CHCl_3$; *ii* HCl

In fact, heating dimethyl ester of hematoporphyrin-IX (**12**) and *tert*-butylphenol in chloroform–carbon tetrachloride solution in the presence of excess* zinc acetate gives first the corresponding zinc complex **13**. This then reacts with *tert*-butylphenol to form the complex **14** which is subsequently demetallated by work up with hydrochloric acid to give the corresponding bis-*tert*-butylphenyl ether **15** in 80-90% yield (Scheme 4).

The reaction with β-diketones occurs readily in the same way. Hence the reaction of porphyrins **12** or **16** [4] with zinc acetate in a solution of acetylacetone gives the zinc complex **17** in high yield (80-90%). Demetallation using hydrochloric acid then gives the corresponding porphyrin **18** (Scheme 5).

Scheme 5

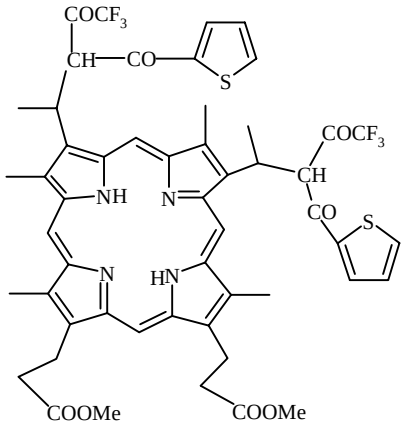


12 R = H; **16** R = Me; *i* $CH_2Ac_2/Zn(OAc)_2$, 100-110°C, 0.5-1 h; *ii* HCl, 2 min

* The amount of zinc acetate corresponds to at least 5 to 10 times the weight amount of porphyrin taken for the reaction.

Porphyrin **18** can be readily prepared from the cheaper and more readily commercially available porphyrin **2**, separated from the natural raw material hematoporphyrin-IX dihydrochloride. In this case the complex formed **19** needs to be converted to the corresponding dimethyl ether **18** by work up with 5% H_2SO_4 in methanol.

Starting from porphyrins **12** and **16** and the β-diketones (dibenzoylmethane, benzoylacetone, or 4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione), other addition products including the porphyrin **20** were obtained by refluxing in carbon tetrachloride in the presence of zinc acetate.



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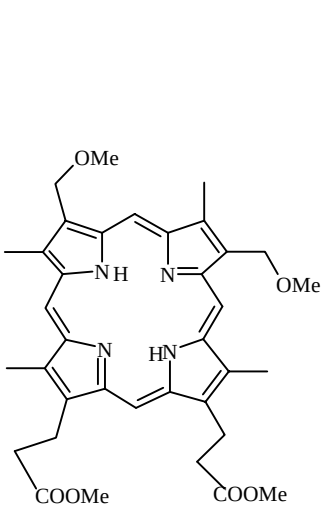
Not only porphyrins containing α-hydroxy(alkoxy)ethyl substituents but also simpler porphyrins with alkoxymethyl peripheral substituents were able to react with β-diketones. Such porphyrins are readily obtained by Friedel-Crafts alkylation of deuterohemin-IX *via* the chloromethyl methyl ether, demetallation in acetic acid containing HBr, and work up with the corresponding alcohol [16]. Hence heating the dimethyl ester of 2,4-di(methoxymethyl)deuteroporphyrin-IX (**21**) with acetylacetone or benzoylacetone in dichloroethane solution with zinc acetate gave the zinc complexes **22** and **23**. It follows that the corresponding porphyrins can then be obtained by demetallation of the zinc complexes **22** and **23** using hydrochloric acid.



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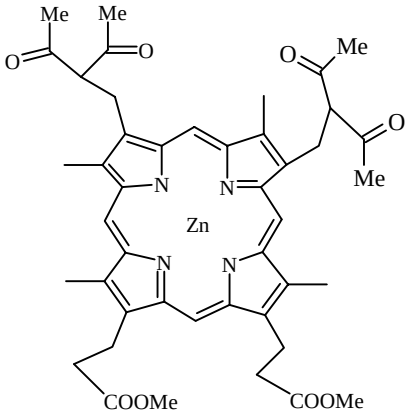

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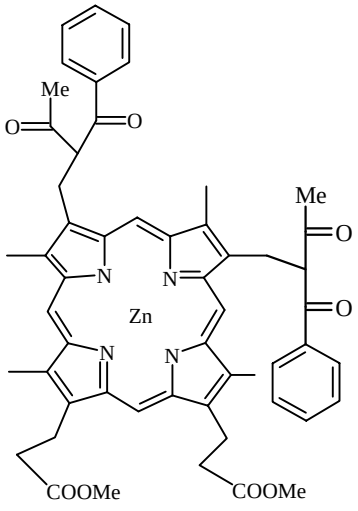

23

^{1}H NMR Spectra. An interesting effect was noted with the β-diketone residues on the proton signals for the C<u>H</u>–C<u>H</u>$_3$ substituent in positions 2 and 4 when compared with the hydroxy(alkoxy) groups in the hematoporphyrin derivative molecules. These signals are strongly broadened and appear in the form of unstructured multiplets at 5.54 and 2.03 ppm. In the porphyrin **16** they appear as a classical quadruplet at 6.05 ppm (C<u>H</u>–CH$_3$) and two well resolved doublets at 2.26 ad 2.25 ppm (CH–C<u>H</u>$_3$) with a spin-spin coupling of 6.0 Hz.

Upon protonation in trifluoroacetic acid these groups of protons show a broad signal at 5.78 ppm and three broad doublets in the region 2.18-2.05 ppm. At the same time, the signals for the protons of the acetyl groups in each of the β-diketone residues appear both in the form of four well resolved signals in the region 2.62-2.60 ppm and as two structureless signals at 1.61 and 1.57 ppm. The presence in the spectrum of two types of signals for the acetyl group protons can be interpreted in the following way. Since the bulky acetylacetonate substituents can be located in the plane of the macrocycle such that one of the acetyl groups is placed to the side of the porphyrin it will be subject to the shielding effect of the ring current to a minimal degree and such acetyl group methyl protons will give singlet signals at relatively low field, i.e., at 2.62-2.60 ppm. The occurrence of four signals of equal intensity is associated with the presence of two chiral centers occurring as the *R*- and *S*- forms in the unsymmetrical molecule **18**. The presence of two broad signals to high field of other acetyl group protons in each of the acetylacetonate residues can be related, in the first place, to the effect of the ring current of the sterically closely placed porphyrin macrocycle and, in the second, to the possible formation of an enol tautomer (to some degree). It is likely that, for the same reason, the C<u>H</u>Ac_2 proton in the acetylacetone residue in the region 5.27 ppm for porphyrin **18** (5.26 ppm for complex **17**) appears as an exceptionally broad, structureless signal. In an example, where the possibility of keto-enol tautomerism can be fully excluded and the acetyl groups are placed symmetrically relative to the plane of the macrocycle (e.g., in *meso*-(2-acetyl-3-oxobutyl)etioporphyrin-I or *meso*-diacetylmethyloctaethylporphyrin) the broad signals for the acetyl residue protons at high field are absent in the ^{1}H NMR spectrum.

Addition of CF_3COOH leads to a low field shift of virtually all of the signals in the ^{1}H NMR spectrum. The highest shift is a feature of the *meso* proton signals (by about 0.9-1.0 ppm) and the C<u>H</u>–CH_3 protons (about 0.5 ppm). Protonation gives rise to a characteristic doubling of the signals for the *meso* protons, the protons of the ring methyl substituents, and the protons of the C<u>H</u>–C<u>H_3</u> groups. In the region 2.3-2.2 ppm there are observed two groups of signals with two doublets in each and this points to the presence of the two *R*- and *S*- forms for the substituents in positions 2 and 4 of the deuteroporphyrin-IX.

Electronic Spectra. Introduction of β-diketonate residues into the porphyrin molecule, either in the *meso* or the peripheral position of the pyrrole rings causes virtually no marked change to the visible part of the electronic spectrum when compared with usual alkyl substituents. However, the presence of aromatic (phenyl or thienyl) residues in the β-diketones is very readily detected in the ultraviolet region of the spectrum in the region 240-260 nm (in which the inherent absorption due to the porphyrin ring is small). Figures 1-3 show the spectra of the porphyrins with aromatic β-diketones. The presence of a *meso* substituent leads to a bathochromic shift of all the usual bands (the Soret band and four bands in the visible part of the spectrum) by 13-16 nm when compared with the spectra of *meso*-unsubstituted porphyrins with similar β-substituents.

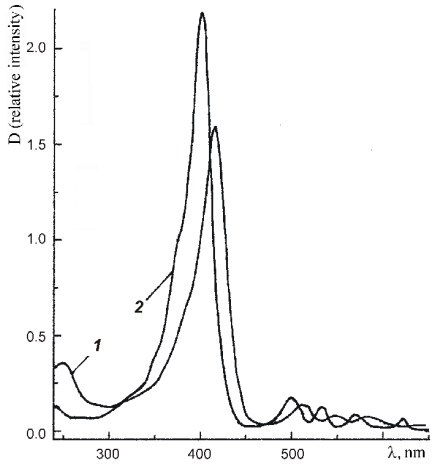

Fig. 1. UV spectra of porphyrins *1*- **9**; *2*- **18**.

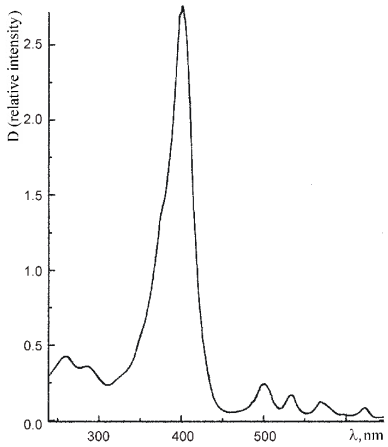

Fig. 2. UV spectrum of porphyrin **20**.

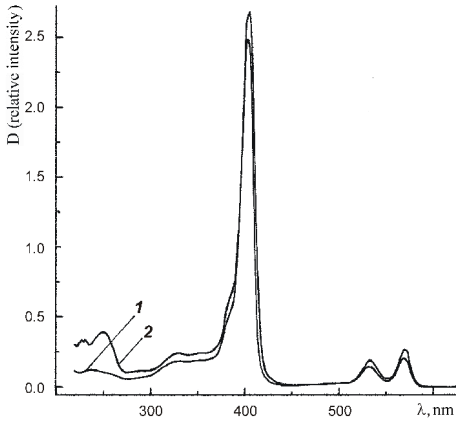

Fig. 3. UV spectra of Zn complexes *1*- **22**; *2*- **23**.

EXPERIMENTAL*

^{1}H NMR spectra were recorded on Bruker WM 360, WP-250, and AC-200 instruments using the signal for $CHCl_3$ as internal standard at 7.26 ppm. Mass spectra of porphyrin derivatives with β-diketones were taken on a Finnigan MAT 90 instrument as described in [9] and for porphyrin **15** using MALDI on a mass spectrometer at the Institute of Laser Medicine at Dusseldorf University, Germany. Electronic spectra were measured on a Hewlett-Packard model 8453 instrument using chloroform (the optical density for each of the absorption bands is given in units relative to one of the bands in the visible part of the spectrum taken as 1.0). Chromatographic separations for the porphyrins were carried out on Merck G 60 silica gel columns (0.040-0.063 mm).

General Method for Preparing Porphyrins 7-9. A solution of porphyrin **5** or **6** (100 mg), dibenzoylmethane or benzoylacetone (500 mg), and $Zn(OAc)_2 \cdot 2H_2O$ (500 mg) in carbon tetrachloride (30 ml) was heated at reflux for 3-4 h until disappearance of the zinc complex of the starting porphyrin from the reaction mixture. Solvent was then removed in vacuo and the residue was washed with hot water, and chromatographed on a silica gel column using chloroform The main fraction was evaporated in vacuo and crystallized from a mixture of methylene chloride and methanol to give the corresponding zinc complexes of the porphyrins in 80-85% yield. A short treatment with hydrochloric acid gave porphyrins **8** and **9** in quantitative yield.

Zinc Complex of *meso*-(2-Benzoyl-3-oxobutyl)octaethylporphyrin (7). ^{1}H NMR spectrum (400 MHz, $CDCl_3$): 9.98, 9.94, 9.88 (3H, all s, *meso*-H); 5.93 and 5.90 (1H, two d, C$\underline{H}_2$–CH); 5.57-5.54 (3H, m C$\underline{H}_2$–CH and *o*-Ph); 4.76 and 4.65 (3H, two t, *m*-Ph, *p*-Ph); 4.54 and 4.51 (1H, two t, CH_2–C$\underline{H}$); 4.2-3.9 (8H, overlapping q, 4 × C$\underline{H}_2$CH$_3$); 1.9-1.85 (18H, overlapping t, 6 × CH_2C$\underline{H}_3$); 1.75 and 1.68 (6H, two t, 2 × CH_2C$\underline{H}_3$); 1.49 ppm (3H, s, COC$\underline{H}_3$). UV spectrum, λ_{max} (relative intensity): 226 (1.29), 247 (1.50), 330 (0.92), 405 (10.34), 533 (0.73), 570 nm (1.00).

***meso*-(2,2-Dibenzoylethyl)etioporphyrin-I (8).** ^{1}H NMR spectrum (400 MHz, $CDCl_3$): 9.93, 9.86, 9.82 (3H, all s, *meso*-H); 6.61 and 6.32 (two d, 2H and 2H, *o*-Ph); 6.07 and 5.87 (two m, C$\underline{H}_2$–CH); 6.05, 5.92, 5.65 and 5.55 (6H, all m, *m*-Ph, *p*-Ph); 5.37 (1H, t, CH_2–C$\underline{H}$); 4.2-3.8 (8H, overlapping q, 4 × C$\underline{H}_2$CH$_3$); 3.53, 3.52, 3.51, 3.49 (12H, all s, 4 × C$\underline{H}_3$ ring); 1.9-1.75 (9H, overlapping t, 3 × CH_2C$\underline{H}_3$); 1.65 (3H, t, CH_2C$\underline{H}_3$); -3.15 and -3.66 ppm (2H, NH). UV spectrum, λ_{max} (relative intensity): 233 (1.68), 249 (1.75), 331 sh (1.25), 412 (13.5), 512 (1.00), 549 (0.56), 583 (0.475), 647 nm (0.21).

***meso*-(2,2-Dibenzoylethyl)octaethylporphyrin (9).** ^{1}H NMR spectrum (400 MHz, $CDCl_3$): 9.87 and 9.81 (2H and 1H, two s, *meso*-H); 6.39 (4H, d, *J* = 7.5 Hz, *o*-Ph); 5.88 (2H, d, *J* = 7.0 Hz, C$\underline{H}_2$CH); 5.82 (2H, t, *J* = 7.2 Hz, *p*-Ph); 5.69 (4H, t, *J* = 7.6 Hz, *m*-Ph); 5.28 (1H, t, *J* = 7.0 Hz, CH_2C$\underline{H}$); 4.10-3.95 (12H, overlapping q, 6 × C$\underline{H}_2$CH$_3$); 3.93 (4H, q, *J* = 7.5 Hz, 2 × C$\underline{H}_2$CH$_3$); 1.95-1.85 (18H, overlapping t, 6 × CH_2C$\underline{H}_3$); 1.76 (6H, t, *J* = 7.5 Hz, 2 × CH_2C$\underline{H}_3$); -3.06 and -3.66 ppm (2H, two s, NH). UV spectrum, λ_{max} (relative intensity): 250 (1.67), 331 sh (1.67), 412 (13.61), 513 (1.00), 549 (0.61), 583 (0.47), 647 nm (0.22).

Dimethyl Ester of 2,4-Di(α-4-*tert*-butylphenoxyethyl)deuteroporphyrin-IX (15). A mixture of dimethyl ester of hematoporphyrin-IX (**12**, 100 mg, 0.2 mmol), *tert*-butylphenol (150 mg), and $Zn(OAc)_2 \cdot 2H_2O$ (250 mg) in a mixture of chloroform (2 ml) and carbon tetrachloride (6 ml) was refluxed for 3 h until complete disappearance of the starting complex **13** from the reaction mixture. Water was added to the solution and the porphyrin was extracted with chloroform. The organic layer was shaken with 15% HCl, washed with water, aqueous ammonia, and then filtered through a 1 cm layer of silica gel. It was concentrated in vacuo to small volume and crystallized by gradual addition of methanol to give porphyrin **15** (116 mg, 82%). ^{1}H NMR spectrum ($CDCl_3$): 10.59, 10.58, 10.57 (2H, all s, α,β-*meso*-H); 10.10, 10.06 (2H, all s, γ,β-*meso*-H); 7.25-6.90 (10H, m, phenyl protons and C$\underline{H}$CH$_3$ protons); 4.50-4.30 (4H, overlapping t, C$\underline{H}_2$CH$_2$COOCH$_3$); 3.80, 3.76, 3.69, 3.68, 3.64 (18H, all s, CH_3 ring and COOC$\underline{H}_3$); 3.35-3.20 (4H, overlapping t, CH_2C$\underline{H}_2$COOCH$_3$); 2.43 (6H, d, *J* = 6.3 Hz, 2 × CHC$\underline{H}_3$); 1.06 (18H, s, 2 × C(CH$_3$)$_3$); -2.62 ppm (2H, br. s, 2 × NH). Mass spectrum (MALDI): 891 (M+H), 740, 590. Calculated for $C_{56}H_{66}N_4O_6$: 890.

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* The experimental section also includes previously unpublished data for the ^{1}H NMR spectra of porphyrins **16** and **21**.

Dimethyl Ester of 2,4-Di(α-methoxyethyl)deuteroporphyrin-IX (16). Prepared by the method described in [4]. ^{1}H NMR spectrum (360 MHz, $CDCl_3$): 10.55, 10.51, 10.13, 10.08 (4H, all s, *meso*-H); 6.05 (2H, q, J = 6.6 Hz, C<u>H</u>–CH_3); 4.42 and 3.30 (8H, two t, 2 × $C\underline{H}_2C\underline{H}_2COOCH_3$); 3.71, 3.67, 3.66, 3.65, and 3.61 (24H, all s, 4 × $C\underline{H}_3$ ring, 2 × $CH(OC\underline{H}_3)$, 2 × $COOC\underline{H}_3$); 2.26 and 2.25 (6H, two d, J = 6.6 Hz, 2 × CH–$C\underline{H}_3$); -3.70 ppm (2H, s, NH). ^{1}H NMR spectrum (360 MHz, $CDCl_3$ + 0.5% CF_3COOD): 11.45, 11.408, 11.407, 11.36, 11.194, 11.19, 11.089 and 11.059 (4H, all s, *meso*-H); 6.43 (2H, m, C<u>H</u>–CH_3); 4.72 (4H, m, 2 × $C\underline{H}_2CH_2COOCH_3$); 3.875, 3.865, 3.728, 3.714, 3.65, 3.642, 3.638, 3.623, 3.613, 3.60, 3.58, 3.542 and 3.538 (24H, all s, 4 × $C\underline{H}_3$ ring, 2 × $COOC\underline{H}_3$, 2 × $CHOC\underline{H}_3$), 3.33 and 3.31 (4H, two t, J = 7.5 Hz, 2 × $CH_2C\underline{H}_2COOCH_3$); 3.71, 3.67, 3.66, 3.65 and 3.61 (24H, all s, 4 × $C\underline{H}_3$ ring, 2 × $CHOC\underline{H}_3$, 2 × $COOC\underline{H}_3$); 2.336, 2.33, 2.24 and 2.22 ppm (6H, all d, J = 6.6 Hz, 2 × CH–$C\underline{H}_3$).

d_6-Dimethyl Ester of 2,4-Di(α-methoxy-d_6-ethyl)deuteroporphyrin-IX (16). Prepared by the method described in [4] using CD_3OD for the methanolysis of perbromide **3.** ^{1}H NMR spectrum (360 MHz, $CDCl_3$); 10.55, 10.51, 10.13. 10.08 (4H, all s, *meso*-H); 6.05 (2H, q, J = 6.6 Hz, C<u>H</u>–CH_3); 4.42 and 3.30 (8H, two t, J = 7.5 Hz, 2 × $C\underline{H}_2C\underline{H}_2COOCH_3$); 3.71 and 3.66 (12H, all s, 4 × $C\underline{H}_3$ ring); 2.26 and 2.25 (6H, two d, J = 6.6 Hz, 2 × CH–$C\underline{H}_3$); -3.70 ppm (2H, s, NH).

Dimethyl Ester of 2,4-[α-(Diacetylmethyl)ethyl]deuteroporphyrin-IX (18). A mixture of the tetramethyl ester of hematoporphyrin-IX (0.5 g) (16) and zinc acetate ($Zn(OAc)_2 \cdot 2H_2O$, 1.5 g) in freshly distilled acetylacetone (50 ml) was heated at 110°C for 1.5 h. The product was evaporated in vacuo, the residue was washed several times with hot water and extracted with chloroform and the material was then chromatographed on a silica gel column. The main fraction was evaporated to small volume (3-5 ml), methanol (25 ml) was added, and the precipitated crystals were filtered off to give complex **17** (0.55 g, 84%). Demetallation with hydrochloric acid gave a quantitative yield of porphyrin **18** after crystallization from a mixture of chloroform and methanol.

Zinc Complex 17. ^{1}H NMR spectrum (360 Mz, $CDCl_3$): 10.29, 10.09, 10.01 (2H, 1H, 1H, all s, *meso*-H); 5.6 (2H, very br. structureless signal, $C\underline{H}(CH_3)CHAc_2$); 5.28 (2H, br. structureless signal, $CH(CH_3)C\underline{H}Ac_2$); 4.40 and 4.32 (2H and 2H, two t, 2 × $C\underline{H}_2CH_2COOCH_3$); 3.82, 3.74, 3.73, 3.69, 3.64, 3.59 (18H, all s, 4 × CH_3 ring and 2 × $COOCH_3$); 3.28 and 3.23 (2H and 2H, two t, 2 × $CH_2C\underline{H}_2COOCH_3$); 2.63, 2.625, 2.605, 2.60 (6H, all s, 2 × $COC\underline{H}_3$); 2.05 (6H, br. s, 2 × $CH(C\underline{H}_3)$); 1.64 and 1.56 ppm (6H, two br. s, 2 × $COC\underline{H}_3$). UV spectrum, λ_{max} (relative intensity): 403 (11.86), 532 (0.71), 569 nm (1.00).

Porphyrin 18. ^{1}H NMR spectrum (360 MHz, $CDCl_3$): 10.25, 10.24, 10.11, 10.10 (4H, all s, *meso*-H); 5.54 and 5.27 (2H, 2H, two structureless m, $C\underline{H}(CH_3)C\underline{H}Ac_2$); 4.44 and 4.42 (2H and 2H, two t, 2 × $C\underline{H}_2CH_2COOCH_3$); 3.80, 3.735, 3.73, 3.67, 3.65, 3.64 (18H, all s, 4 × CH_3 ring and 2 × $COOCH_3$); 3.30 and 3.28 (2H and 2H, two t, 2 × $CH_2C\underline{H}_2COOCH_3$); 2.626, 2.624, 2.61, 2.606 (6H, all s, $COC\underline{H}_3$); 2.03 (6H, structureless m, 2 × $CH(C\underline{H}_3)$); 1.61 and 1.57 (3H and 3H, two structureless m, $COC\underline{H}_3$); -3.76 ppm (2H, s, NH). ^{1}H NMR spectrum (in CF_3COOD): 11.28, 11.27, 11.25, 11.245, 11.195, 11.19 (3H, all s, *meso*-H); 11.01 (1H, s, *meso*-H); 5.78 (2H, br. structureless m, $C\underline{H}(CH_3)CHAc_2$); 5.65 and 5.63 (1H, two d, J = 7 Hz, $C\underline{H}Ac_2$); 5.64 and 5.59 (1H, two d, J = 11 Hz, $C\underline{H}Ac_2$); 4.71, 3.30 (8H, two t, 2 × $C\underline{H}_2C\underline{H}_2COOMe$); 4.01, 4.00, 3.97, 3.96 (6H, all s, 2 × $C\underline{H}_3$ ring); 3.87 and 3.80 (6H, two s, 2 × $C\underline{H}_3$ ring); 3.81 and 3.77 (6H, two s, 2 × $COOC\underline{H}_3$); 2.90, 2.89, 2.89, 2.855 (6H, all s, 2 × $COC\underline{H}_3$); 2.18, 2.11, 2.05 (6H, all br. d, J = 6.0 Hz, 2 × CH–$C\underline{H}_3$); 2.05, 2.03, 1.96, 1.92 ppm (6H, all br. s, 2 × $COC\underline{H}_3$). UV spectrum, λ_{max} (relative intensity): 375 sh (5.44), 401 (12.16), 500 (1.00), 533 (0.67), 569 (0.89), 623 nm (0.35).

Dimethyl Ester of 2,4-Di(methoxymethyl)deuteroporphyrin-IX (21). Prepared by the method described in [16]. ^{1}H NMR spectrum (360 MHz, $CDCl_3$): 10.24, 10.20, 10.08 and 10.05 (4H, all s, *meso*-H); 5.89 and 5.88 (2H, 2H, two s, 2 × $C\underline{H}_2O$); 4.40 (4H, t, J = 7.5 Hz, 2 × $C\underline{H}_2CH_2COOCH_3$); 3.73, 3.72, 3.69, 3.68, 3.67 and 3.63 (3H, 3H, 3H, 3H, 6H, 6H, all s, 2 × $COOC\underline{H}_3$, 2 × $CH_2OC\underline{H}_3$ and 4 × CH_3 ring); 3.28 (4H, t, J = 7.5 Hz, 2 × $CH_2C\underline{H}_2COOCH_3$); -3.71 ppm (2H, br. s, $NH_{porphyrin}$). UV Spectrum, λ_{max} (relative intensity): 400 (11.58), 499 (1.00), 533 (0.68), 570 (0.47), 622 nm(0.31).

Zinc Complex of Dimethyl Ester of 2,4-Di(2-acetyl-3-oxobutyl)deuteroporphyrin-XI (22). ^{1}H NMR spectrum (200 MHz, $CDCl_3$): 9.44, 9.19, 9.14 and 8.75 (4H, all s, *meso*-H); 4.50-3.90 (10H, m, 2 × $C\underline{H}_2C\underline{H}$ and 2 × $C\underline{H}_2CH_2COOCH_3$); 3.69, 3.66, 3.41, 3.39, 3.17 and 3.13 (18H, all s, 2 × $COOC\underline{H}_3$ and 4 × $C\underline{H}_3$ ring); 3.13 (4H, m, 2 × $CH_2C\underline{H}_2COOCH_3$); 1.99 and 1.90 ppm (12H, s, 4 × $COC\underline{H}_3$). UV spectrum, λ_{max} (relative intensity): 236 (0.60), 329 (9.90), 380 sh (2.09), 403 (11.85), 533 (0.714), 569 nm (1.00).

Zinc Complex of Dimethyl Ester of 2,4-Di(2-benzoyl-3-oxobutyl)deuteroporphyrin-XI (23). ^{1}H NMR spectrum (200 MHz, $CDCl_3$): 9.27, 9.03, 8.93 and 8.50 (4H, all s, *meso*-H); 7.70-6.80 (10H, m, 2 × Ph); 5.12 and 4.98 (2H, t, J = 6.5 Hz, 2 × $CH_2C\underline{H}$); 4.35-4.00 (8H, m, 2 × $C\underline{H}_2CH$ and 2 × $C\underline{H}_2CH_2COOCH_3$); 3.68, 3.64, 3.34, 3.29, 3.03 and 2.97 (18H, all s, 2 × $COOC\underline{H}_3$ and 4 × $C\underline{H}_3$ ring); 3.08 (4H, t, J = 7.5 Hz, 2 × $CH_2C\underline{H}_2COOCH_3$); 2.09, 2.06 and 1.96 ppm (6H, all s, 2 × $COC\underline{H}_3$). UV spectrum, λ_{max} (relative intensity): 226 (1.23), 248 (1.46), 328 (0.94), 405 (10.31), 533 (0.73), 571 nm (1.00).

Dimethyl Ester of 2,4-Di[1-methyl-2-trifluoroacetyl-2-(2-thenoyl)ethyl]deuteroporphyrin-XI (20). ^{1}H NMR spectrum (250 MHz): 10.28, 10.27, 10.09, 10.08 (4H, all s, *meso*-H); 7.76, 7.54, 6.98 (2H, 2H, 2H, all m, thienyl 4-, 2- and 3-protons); 5.37 (4H, m, $C\underline{H}(CH_3)C\underline{H}COCF_3$); 4.08, 3.29 (4H, 4H, two m, 2 × $C\underline{H}_2C\underline{H}_2COOCH_3$); 3.79, 3.78, 3.75, 3.68, 3.67, 3.645, 3.64 (18H, all s, 4 × $C\underline{H}_3$ ring and 2 × $COOC\underline{H}_3$); 2.23, 2.20 (3H, 3H, d, 2 × CH–$C\underline{H}_3$); -3.78 ppm (1H, s, NH). UV spectrum, λ_{max} (relative intensity): 260 (1.8), 285 (1.48), 372 sh (5.36), 402 (11.12), 499 (1.00), 533 (0.64), 568 (0.50), 596 sh (0.16), 621 nm (0.336).

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