10-Hydroxy-3,10-dimethyl-2,3,4,10-tetrahydropyrimido[1,2-a]indole (VIII). A 6.1-g (0.04 mole) sample of phosphorus oxychloride was added to a solution of 4.65 g (0.02 mole) of 4-methyl-1-phenyl-2-isobutyrylpyrazolidine [1] in 50 ml of absolute benzene, after which the mixture was refluxed for 60 h. The resulting precipitate was removed by filtration and dissolved in water. The solution was made alkaline to pH ~9, and the product was extracted with ether. The precipitate that formed from the ether solution on standing was separated and recrystallized from benzene–heptane to give 1.55 g (36%) of VIII with mp 228-230°. No melting-point depression was observed for a mixture of this product with a genuine sample [1], and their IR and PMR spectra were completely identical.

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PORPHYRINS

III.* SYNTHESIS AND PROPERTIES OF PORPHYRINS WITH HYDROXYALKYL SUBSTITUENTS

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The corresponding porphyrin was synthesized from 1-bromo-2,7,13,17,19-pentamethyl-3,8-diethyl-12-[2-(methoxycarbonyl)ethyl]bila-a,c-diene. Cyclization of the biladiene in dimethyl sulfoxide is accompanied by bromination of the β position of the porphyrin. Treatment of some porphyrins containing an ester grouping with sodium borohydride leads to reduction of the latter. The reduction products in concentrated sulfuric acid form sulfates that exist in the stable "monocation" form.

Of the porphyrins that have appreciable pharmacological activity most study has been devoted to hematoporphyrin IX [2], which contains two α-hydroxyethyl substituents and two β-carboxyethyl substituents. In order to study the biological and physicochemical properties of porphyrins containing such substituents we synthesized a model porphyrin (I) from pyrroporphyrin methyl ester (II). Starting II was obtained by cyclization of bila-a,c-diene V, synthesized from dipyrrylmethenes III and IV, in o-dichlorobenzene or in dimethyl sulfoxide (DMSO)–pyridine by the method in [3, 4]. [See structure on top of next page.]

Whereas the cyclization of biladiene V in o-dichlorobenzene took place in conformity with the methods described in [3], the result of cyclization in DMSO–pyridine depended to a considerable degree on the method used to isolate the final product. Thus maintenance of V at room temperature for 3-4 days gave porphyrin II, which was isolated from the reaction mixture in 70-75% yield. A new porphyrin, a characteristic feature of which was the absence of fluorescence in UV light, was obtained when the cyclization was carried out above 80°C with access to air for several hours with subsequent vacuum evaporation of the reaction mixture. Analysis of the PMR and mass spectral data made it possible to unambiguously establish that the product was

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[*] See [1] for communication II.

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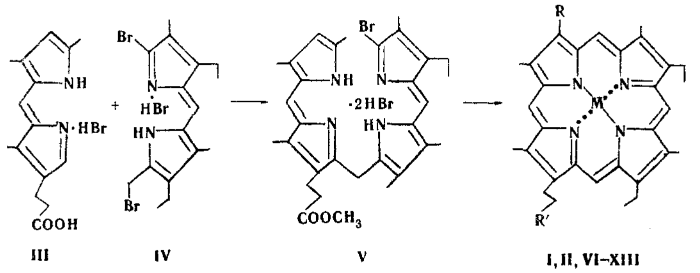

I $R=CH(OH)CH_3$, $R'=COOCH_3$, $M=2H$; II $R=H$, $R'=COOCH_3$, $M=2H$; VI $R=Br$, $R'=COOCH_3$, $M=2H$; VII $R=H$, $R'=COOCH_3$, $M=Cu$; VIII $R=COCH_3$, $R'=COOCH_3$, $M=Cu$; IX $R=COCH_3$, $R'=COOCH_3$, $M=2H$; X $R=CH(OH)CH_3$, $R'=CH_2OH$, $M=2H$; XI $R=H$, $R'=CH_2OH$, $M=2H$; XII $R=H$, $R'=CH_2OSO_3H$, $M=2H$; XIII $R=H$, $R'=CH_2OCOCH_3$, $M=2H$

2-bromopyrroporphyrin (VI). The molecular ion peaks with m/e 586 and 588 were the most intense peaks in the mass spectrum, and this result was in agreement with the introduction of bromine in the porphyrin ring. The signal of a β proton at δ 8.94 ppm was absent in the PMR spectrum of this porphyrin, whereas signals of meso protons were retained; all four meso protons were nonequivalent. Thus the presence of bromine leads to rather pronounced shielding of one of the meso protons (9.54 ppm) as compared with the meso protons of porphyrin II [9.85 (1H) and 9.95 ppm (3H)].

In order to ascertain the stage of the cyclization at which the pyrrole ring is brominated, we carried out a series of experiments. It was found that exclusively the nonbrominated product is formed during cyclization under argon at temperatures up to 130°. The bubbling in of even a very weak stream of air at temperatures above 80° leads to bromoporphyrin VI. Compound VI is obtained in quantitative yield when porphyrin II is heated under similar conditions in the presence of a tenfold excess of HBr. Consequently, the phenomenon of bromination of the β-unsubstituted position of the porphyrin ring that we observed in this study takes place in the step involving the formation of the porphyrin. It may be assumed that in the presence of air at high temperatures DMSO is readily decomposed to dimethyl sulfide and atomic oxygen, which oxidizes the hydrogen bromide present in the reaction mixture to free bromine. The latter in turn, in the form of an adduct with pyridine, is a reagent that selectively brominates only the β-unsubstituted position of the porphyrin ring, inasmuch as meso-bromoporphyrins were not detected in the reaction mixture.

It is well known [5] that the most convenient method for the preparation of porphyrins with α-hydroxyethyl substituents is reduction of the corresponding acetylporphyrins with sodium borohydride. In order to subsequently convert II to I, we therefore acetylated the copper complex (VII) of porphyrin II with acetic anhydride in the presence of stannic chloride in chloroform, after which we subjected complex VIII to demetallation by treatment with concentrated sulfuric acid.

In the reduction of acetylporphyrin IX we observe that the direction of the reduction depends to a considerable degree on the solvent [6]. Maintenance of IX at room temperature in tetrahydrofuran (THF) in the presence of excess sodium borohydride for 4 h leads to simultaneous reduction of both the acetyl and ester groups to give porphyrins I and X in 33.2 and 32.6% yields, respectively; the yield of X was 91% after 12 h. Starting porphyrin II was also readily converted to (γ-hydroxypropyl)porphyrin in high yield.

Bands of the stretching vibrations of the carbonyl group of ester and acetyl groups are absent in the IR spectra of porphyrins X and XI, whereas additional multiplets from the middle CH_2 group of the propyl alcohol residue appear at strong field in the PMR spectra (see Table 1).

In order to solve the problem of the possibility of reduction of the ester groups of the propionic acid residues in other porphyrins, we treated deuteroporphyrin IX dimethyl ester with sodium borohydride under the same conditions. It was found that this reduction gives only a small yield of product. A model compound – ethyl hydrocinnamate – also was not reduced.

On the basis of these facts it may be concluded that the reduction of the ester groups in porphyrin by sodium borohydride is due, in addition to the activating effect of the porphyrin ring, to the mutual orientation and composition of its side substituents.

The acetyl group in porphyrin IX is selectively reduced in dimethylformamide (DMF) or pyridine.

An interesting peculiarity of porphyrins X and XI was the unexpected ready formation of sulfates when they were dissolved in the cold in concentrated sulfuric acid. These compounds are practically insoluble in chloroform and other low-polarity solvents. According to the results of thin-layer chromatography (TLC), the

TABLE 1. PMR Spectra of Porphyrins*

Compound	meso-H	CH_3	C_2H_5 (J, Hz)		$-CH_2-CH_2CO-$ (J, Hz)	OCH_3	R	N–H
			CH_2	CH_3				
II	9,87 (1) 9,95 (3)	3,52 3,54 3,59 3,63	3,99 (8,0) 3,96 (8,0)	1,80 1,75	4,33 3,17 (8,0)	3,50	β-H 8,94	−3,94
I	9,61 9,83 9,86 9,88	3,32 3,32 3,47 3,55	3,92 (7,5) 3,94 7,5	1,76 1,79	4,18 3,12 (8,0)	3,11	CH_3 1,84 $-\overset{\vert}{\underset{\vert}{C}}-H$ 5,78 (6,0)	
VI	9,54 9,74 9,76 9,88	3,33 3,33 3,43 3,47	3,89 (7,5)	1,73	4,23 3,08 (7,5)	3,55		−4,48
IX	9,81 9,84 9,87 10,66	3,55 3,60 3,60 3.75	3,97 (7,5)	1,77	4,30 3,17 (8,0)	3,21	$COCH_3$ 3,46	
X†	10,51 10,51 10,62 11,12	3.51 3,53	4,01 (7,3) 4,08 (7,3)	2,35 2,36	$-CH_2-CH_2-CH_2-$ 4,41 3,43 2,33		CH_3 2,13 $-\underset{\vert}{\overset{\vert}{C}}H$ 6,47 OH 8,01 (6,8)	
XI†	10,52 10,52 10,56 10,70	3,58 3,58 3,58 3,67	4.04 (7,5) 4,18 (7,5)	1,61 1,65	4,10 3,32 2,17 (6,0) (8,0)		β-H 9,25 —OH 7,82	

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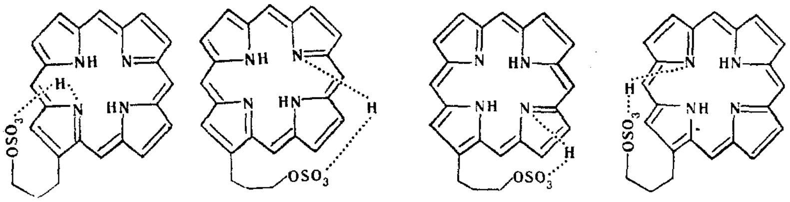
* The PMR spectra were obtained from $CDCl_3$ solutions; the chemical shifts in parts per million are presented on the δ scale.

† The spectra were recorded from solutions in $CDCl_3$ containing 1% CF_3COOH.

sulfates were stable in methanol and pyridine, while treatment of them with 5% sulfuric acid in methanol leads to regeneration of alcohols X and XI.

In an investigation of the electronic spectrum of sulfate XII it was observed that in chloroform solution in the presence of small amount of methanol this compound exists in the form of a stable cyclic inner salt in the form of a "monocation" due to protonation of one of the pyrrole nitrogen atoms by a sulfuric acid residue. It is known [7] that in the protonated form the porphyrin cation and the acid anion interact strongly through a hydrogen bond. Consequently, it may be assumed that one of the following four fixed structures is realized in the crystalline state when an unsymmetrically substituted porphyrin with a substituent with a certain chain length containing a sulfate group is present:



At the same time, an intermediate structure for which charge delocalization between four nitrogen atoms due to rapid NH-tautomerization is characteristic seems most likely in solution. The addition of methanol leads to gradual disruption of the inner salt and to the formation of porphyrin in the free base form.

Rather intense molecular ion peaks are observed in the mass spectra of the investigated porphyrins. Porphyrins I and X, which contain α-hydroxyethyl groups, constitute an exception to this. Despite the fact that the primary hydroxyl group in porphyrins X and XI is separated from the porphyrin ring by a long aliphatic chain, its decomposition is determined to a considerable degree by the effect of porphyrin. In this connection, it seemed of interest to compare the peculiarities of the mass spectrometric behavior of XI and γ-phenylpropyl alcohol.

The following intense ion peaks [m/e (%)] are observed in the mass spectrum of γ-phenylpropyl alcohol: M^+ 136 (20.9), 118 (76.8), 117 (89.6), 105 (19.2), 103 (12.8), 92 (58.9), and 91 (100). As seen from these data, the tropylium ion, with m/e 91, has the maximum intensity. An intense $(M-H_2O)^+$ ion peak with m/e 118 is also observed. The $(M-H_2O)^+$ ion peak is absent in the mass spectrum of alcohol XI, in which the phenyl ring is replaced by the porphyrin ring. It should be noted that the introduction of a porphyrin ring in the aliphatic alcohol molecule considerably increases the stability of the molecular ion, which in this system has the maximum intensity. The behavior of the corresponding acetate (XIII) does not differ from the behavior of free alcohol XI.

The mass spectrum of sulfate XII does not contain a molecular ion peak; the $(M-H_2SO_4)^+$ ion peak is the most intense peak in the spectrum. The formation of this ion is probably associated with thermal splitting out of a molecule of sulfuric acid in the ion source of the mass spectrometer to give the corresponding propenyl derivative. In this case the stable porphyrinylpropylene ion recalls the phenylpropylene ion formed after elimination of a molecule of water.

A low-intensity molecular ion peak is observed in the mass spectrum of porphyrin I. The peak of the $(M-H_2O)^+$ ion, which is the vinyl-porphyrin ion and decomposes with splitting out of CH_3 or CH_2COOCH_3 groups, has the maximum intensity. The $(M-H_2O-CH_3-CH_2COOCH_3)^+$ ion is also observed in the spectrum.

EXPERIMENTAL

The electronic spectra were recorded with a Shimadzu MPS-50L spectrophotometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The mass spectra were recorded with an LKB-9000 spectrometer with introduction of the samples into the ion source of the mass spectrometer. The PMR spectra of the compounds were recorded with a Varian HA-100D spectrometer with hexamethyldisiloxane as the internal standard.

1-Bromo-2,7,13,17,19-pentamethyl-3,8-diethyl-12-[2-(methoxycarbonyl)ethyl]bila-a,c-diene Dihydrobromide (V). A 0.4-ml sample of stannic chloride was added to a mixture of 338 mg of 3,3',5'-trimethyl-4-(2-carboxyethyl)dipyrrylmethene (III) [8] and 480 mg of 5-bromo-5'-bromomethyl-4,3'-dimethyl-4',3-diethyldipyrrylmethene (IV) [9] in 12 ml of nitromethane, after which the mixture was allowed to stand for 1 h. The solvent was then vacuum evaporated, and 10 ml of methanol was added to the residue. After the solid material had dissolved, 1.5 ml of 48% hydrobromic acid was added. After 2-3 h, the precipitated crystals were removed by filtration and washed with a small amount of methanol and ether to give 474 mg (64%) of biladiene with mp > 200° (dec.). Electronic spectrum in chloroform containing 1% HBr, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 456 (34.8) and 530 (158.4). Found %: N 7.5. $C_{32}H_{39}BrN_4O_2 \cdot 2HBr$. Calculated %: N 7.4.

1,3,5,8-Tetramethyl-4,6-diethyl-7-[2-(methoxycarbonyl)ethyl]porphyrin (II). A) A 220-mg sample of biladiene V was refluxed in 250 ml of o-dichlorobenzene for 40 min, after which the solvent was vacuum evaporated. The dry residue was treated with a mixture of 3 ml of concentrated sulfuric acid and 60 ml of methanol. After 12 h, the mixture was diluted with water and neutralized to pH 7-8 with ammonium hydroxide. The product was extracted with chloroform and chromatographed with a column filled with aluminum oxide to give 88 mg (59%) of the porphyrin with mp 258-260° (chloroform–methanol) (mp 248° [10]). Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 402 (234), 500 (17.35), 532 (11.22), 567 (7.75), and 619 (5.1). IR spectrum, ν, cm^{-1}: 3320 and 1743. Mass spectrum, m/e (%): M^+ 508 (100), 493 (9.4), 477 (3.7), 449 (5.4), 435 (21.7), 420 (8.1). Found %: C 75.3; H 7.2; N 11.0. $C_{32}H_{36}N_4O_2$. Calculated %: C 75.6; H 7.1; N 11.0.

B) A mixture of 60 mg of biladiene V, 10 ml of DMSO, and 0.2 ml of pyridine was allowed to stand at room temperature for 48 h, after which 50 ml of water was added, and the resulting precipitate was removed by filtration. The product was dissolved in chloroform and chromatographed with a column filled with aluminum oxide. Crystallization from chloroform–methanol gave 30.1 mg (74%) of a porphyrin with mp 258-260°, which was identical to the sample obtained by method A.

2-Bromo-1,3,5,8-tetramethyl-4,6-diethyl-7-[2-(methoxycarbonyl)ethyl]porphyrin (VI). Air was bubbled for 40 min through a heated (100°) solution of 50 mg of V in 8 ml of DMSO and 0.2 ml of pyridine, after which the mixture was poured into 50 ml of water, and the resulting precipitate was removed by filtration. The product was chromatographed with a column filled with aluminum oxide and eluted with chloroform, and the eluted product was crystallized from chloroform–methanol to give 22.1 mg (57%) of the porphyrin with mp > 300°. Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 504 (15.3), 538 (13.9), 567 (8.6), 620 (2.9). Mass spectrum, m/e (%): M^+ 586, 588 (100), 571, 573 (7.7), 513, 515 (14.1), 498, 500 (5.2). Found %: C 65.6; H 6.0; N 9.6. $C_{32}H_{35}BrN_4O_2$. Calculated %: C 65.4; H 6.0; N 9.5.

Copper Complex (VII) of II. This complex, with mp 252° (from chloroform–methanol), was obtained in quantitative yield from porphyrin II by heating in chloroform in the presence of copper acetate. Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 400 (212), 525 (6.98), 562 (11.85). Found %: C 67.1; H 6.2; N 10.1. $C_{32}H_{34}CuN_4O_2$. Calculated %: C 67.4; H 6.0; N 9.8.

Copper Complex (VIII) of 1,3,5,8-Tetramethyl-4,6-diethyl-2-acetyl-7-[2-(methoxycarbonyl)ethyl]porphyrin. A 57-mg sample of complex VII was dissolved in 16 ml of dry chloroform, after which the solution was cooled, and 3 ml of acetic anhydride and 0.4 ml of stannic chloride were added. The mixture was allowed to stand for 5 min until a green coloration appeared, after which 50 ml of water was added. The chloroform layer was washed with ammonium hydroxide and water until it was neutral, after which it was dried with sodium sulfate and chromatographed with a column filled with aluminum oxide to give 59.5 mg (97%) of a complex with mp 228-230° (from chloroform–methanol). Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 411 (237), 539 (9.2), 585 (17.4). IR spectrum, ν, cm^{-1}: 1740 and 1660. Found %: C 66.7; H 6.3; N 9.0. $C_{34}H_{36}CuN_4O_3$. Calculated %: C 66.7; H 5.9; N 9.1.

1,3,5,8-Tetramethyl-4,6-diethyl-2-acetyl-7-[2-(methoxycarbonyl)ethyl]porphyrin (IX). This compound, with mp 243-245° (from chloroform–methanol), was obtained in 91% yield by treatment of complex VIII with concentrated sulfuric acid. Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 413 (201), 512 (9.62), 552 (12.53), 577 (8.24), 635 (1.66). Mass spectrum, m/e (%): M^+ 550 (100), 535 (79.5), 477 (85.9), 462 (71.5), 447 (49.8), 433 (51.5). Found %: C 74.4; H 7.0; N 10.2. $C_{34}H_{38}N_4O_3$. Calculated %: C 74.2; H 7.0; N 10.2.

1,3,5,8-Tetramethyl-4,6-diethyl-2-(α-hydroxyethyl)-7-[2-(methoxycarbonyl)ethyl]porphyrin (I). A 25.9-mg sample of porphyrin IX was dissolved in 50 ml of pyridine, after which 300 mg of sodium borohydride was added, and the mixture was allowed to stand at 50° for 4 h. Water (100 ml) was added to the mixture, and the product was extracted with chloroform. The chloroform layer was washed repeatedly with water, after which it was dried with magnesium sulfate, and the solvent was removed in vacuo. The dry residue was treated with a mixture of 1.2 ml of concentrated sulfuric acid and 25 ml of methanol. After 12 h, the reaction mixture was diluted with water and neutralized to pH 7-8 with ammonium hydroxide. The product was extracted with chloroform and chromatographed with a column filled with aluminum oxide to give 16 mg (62%) of the porphyrin with mp 235-238° (from chloroform–methanol). Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 404 (179), 502 (12.62), 535 (8.75), 570 (6.0), 621 (3.9). IR spectrum, ν, cm^{-1}: 3400, 3320, and 1740. Mass spectrum, m/e (%): M^+ 552 (4.8), 534 (100), 519 (7.8), 461 (19.3), 446 (7.8). Found %: C 74.2; H 7.3; N 10.0. $C_{34}H_{40}N_4O_3$. Calculated %: C 73.9; H 7.3; N 10.1.

1,3,5,8-Tetramethyl-4,6-diethyl-2-(α-hydroxyethyl)-7-(γ-hydroxypropyl)porphyrin (X). A 20.1-mg sample of porphyrin IX was dissolved in 30 ml of THF, after which 400 mg of sodium borohydride and 0.1 ml of water were added, and the mixture was heated at 50° for 5 min. It was then allowed to stand at room temperature for 12 h, after which it was poured into 100 ml of water. The resulting precipitate was removed by filtration, dried, and chromatographed with a column filled with aluminum oxide to give 17.4 mg (91%) of the porphyrin with mp 227-228° (from chloroform–petroleum ether). Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 404 (183.8), 504 (11.48), 536 (8.57), 570 (5.65), 621 (3.46). IR spectrum, ν, cm^{-1}: 3400 and 3320. Mass spectrum, m/e (%): $(M-H_2O)^+$ 506 (100), 491 (9.5), 461 (16.5), 446 (7), 431 (5.9), 417 (4.7). Found %: C 75.3; H 7.7; N 10.9. $C_{35}H_{40}N_4O_2$. Calculated %: C 75.5; H 7.7; N 10.7.

1,3,5,8-Tetramethyl-4,6-diethyl-7-(γ-hydroxypropyl)porphyrin (XI). A 12.4-mg sample of II was dissolved in 10 ml of THF, after which 260 mg of sodium borohydride and 0.1 ml of water were added, and the mixture was heated at 50° for 1 min. It was then allowed to stand at room temperature for 12 h, after which it was diluted with water, and the resulting precipitate was removed by filtration and chromatographed to give 9.6 mg (83%) of the porphyrin with mp 248-250° (from chloroform–methanol). Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 401 (196), 500 (12.28), 533 (8.15), 567 (5.48), 619 (3.7). IR spectrum, ν, cm^{-1}: 3450 and 3325. Mass spectrum, m/e (%): M^+ 480 (100), 435 (15). Found %: C 77.5; H 7.6; N 11.9. $C_{31}H_{36}N_4O$. Calculated %: C 77.5; H 7.6; N 11.7.

1,3,5,8-Tetramethyl-4,6-diethyl-7-(γ-acetoxypropyl)porphyrin (XIII). A 24-mg sample of alcohol XI was dissolved in 8 ml of pyridine, after which 3 ml of acetic anhydride was added. After 1 h, the mixture was poured into 50 ml of water, and the resulting precipitate was chromatographed with a column filled with aluminum oxide to give 20.9 mg (80%) of the porphyrin with mp 213-215° (from chloroform–methanol). Spectrum in chloroform, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 400 (282), 499 (17.47), 532 (10.58), 568 (7.56), 619 (4.71). IR spectrum, ν: 1740 cm^{-1}. Mass spectrum, m/e (%): M^+ 522 (100), 507 (6.4), 479 (2.2), 462 (3.2), 447 (3.2), 435 (14.8), 420 (6.4). Found %: C 75.5; H 7.1; N 10.6. $C_{33}H_{38}N_4O_2$. Calculated %: C 75.8; H 7.3; N 10.7.

Sulfate (XII) of XI. A 13.8-mg sample of alcohol XI was dissolved in 5 ml of concentrated sulfuric acid, and the mixture was allowed to stand for 2 h, after which it was poured over ice. The aqueous mixture was neutralized to pH 4-5 with ammonia, and the resulting precipitate was removed by filtration and dried to give

9.8 mg (61%) of the porphyrin with mp > 200° (dec.). Spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$), in methanol: 398 (140), 498 (9.2), 530 (6.18), 565 (4.6), 617 (2.76). In chloroform containing 10% methanol: 415 (162), 531 (5.7), 555 (9.4), 598 (3.22). In chloroform containing 0.1% HCl: 416 (176), 553 (11.0), 594 (4.6). Mass spectrum, m/e (%): $(M-H_2SO_4)^+$ 462 (100), 447 (20), 435 (8), 417 (4.7).

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SYNTHESIS AND THREE-DIMENSIONAL STRUCTURE OF THE BENZOATES AND p-NITROBENZOATES OF THE GEOMETRICAL ISOMERS OF SUBSTITUTED 4-HYDROXYPIPERIDINES

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The corresponding stereoisomeric p-nitrobenzoates were obtained by reaction of the geometrical isomers of 1,3-dimethyl-, 1,2,5-trimethyl-, and 1-tert-butyl-3-methyl-4-hydroxypiperidines with p-nitrobenzoyl chloride. The stereoisomers of the corresponding benzoates were also synthesized from the geometrical isomers of 1,3-dimethyl-4-hydroxypiperidines. The primary conformations of the investigated compounds in solution were established by means of their PMR spectra.

In the development of our research on the interrelationship between the structure and the physicochemical characteristics of substituted piperidines [1, 2] we found it necessary to ascertain the primary conformations of the p-nitrobenzoates of the geometrical isomers of substituted 4-hydroxypiperidines. With this end in mind, we synthesized the p-nitrobenzoates of 1-methyl- (I), 1-tert-butyl-3-methyl- (IIβ, γ), 1,3-dimethyl- (IIIβ, γ), and 1,2,5-trimethyl-4-hydroxypiperidines (IVβ, γ) and established their primary conformations in solution.

We used the previously described geometrical isomers of the corresponding 4-hydroxypiperidines [3-6] as the starting compounds for the synthesis of p-nitrobenzoates I-IV.

In conformity with the configuration of the geometrical isomers of the starting 4-hydroxypiperidines [4-6], II-IV were subdivided into two configurational series (the β and γ isomers) as a function of the mutual orientation and spatial orientation of the substituents attached to C_3 and C_4. The acyloxy group attached to C_4 in geometrical isomers IIγ-IVγ is in the cis position with respect to the adjacent methyl group attached to C_3 in IIγ

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