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Synthesis and Basic Properties of 5-Aza-2,3,7,8,12,13,17,18-octamethylporphyrin

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Abstract—5-Aza-2,3,7,8,12,13,17,18-octamethylporphyrin was synthesized and its basic properties were studied by means of spectrophotometric titration. Protonation of nitrogen atoms in the tetrapyrrolic macrocycle with the ethanolic sulfuric acid is found to be a two-step process. Corresponding ionization constants and the concentration ranges of existence of mono- and dicationic forms of the azaporphyrin under investigation are evaluated.

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Recognition and selective binding of anions in solutions is an important problem of modern chemistry and the material sciences. Analysis of the reported data [1–5] shows that with the purpose of creation of molecular devices for detecting anions the polypyrrole macrorings are widely investigated. In such system the anion is bound due to formation of several H-bonds with the proton-donating NH-groups of the pyrrole rings. A characteristic example is evaluation of the anion concentrations in solutions using such fluorescent dye as 3,12,13,22-tetraethyl-8,17-bis-[di-(hydroxyethyl)aminocarbonylethyl]-2,7,18,23-tetramethylsapphyrin. The faults of this method are the relatively low sensitivity and the narrow range of the substrate concentrations (10^{-3}–10^{-1} M) that can be evaluated.

We have offered prevoiusly [6] to use the protonated forms of porphyrins as the receptors for the halide ions (Hal^-). In part, it was shown by means of the direct titration of 3,7,13,17-tetramethyl-2,8,12,18-tetrabutylporphyrines mono (H_3P^+) and dications (H_4P^{2+})with the solutions of halide salts that therewith stable $H_4P^{2+}\cdot Hal^-$ and $H_4P^{2+}\cdot 2Hal^-$ complexes are formed in acetonitrile. On the basis of analysis of the dependences of the fluorescence intensity and lifetime on the concentration of iodide ions in solution was offered to use H_4P^{2+} as a molecular fluorescent receptor of the halide ions [7]. The method developed permits to detect the halide ions in the substrate concentration range 10^{-6}–10^{-1} M that exceeds significantly the level of the above-mentioned analog on the basis of neutral sapphyrin derivative [1].

In the presented work with the purpose of enhancing sensitivity and extending the range of the evaluated concentrations of halide ions in solutions we synthesized 5-aza-2,3,7,8,13,17,18-octamethylporphyrin and studied its basic properties in the solutions of sulfuric acid in ethanol. The process of protonation of nitrogen atoms of the tetrapyrrole macroring is shown to proceed in two steps at the intracyclic nitrogen atoms [Eqs. (1), (2)].

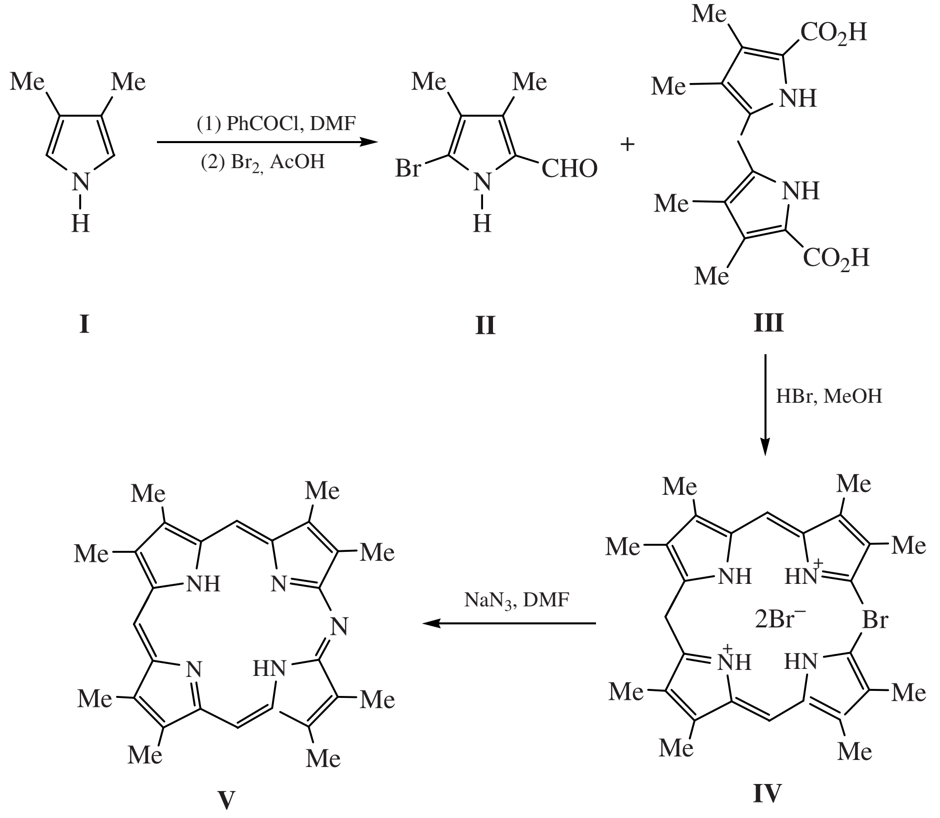
$$H_2P + H^+ \underset{}{\overset{k_{b1}}{\rightleftarrows}} H_3P^+, \qquad (1)$$

$$H_3P^+ + H^+ \underset{}{\overset{k_{b2}}{\rightleftarrows}} H_4P^{2+}. \qquad (2)$$

Here H_2P, H_3P^+, and H_4P^{2+} are the molecular, mono-, and diprotonated forms of corresponding porphyrin. The concentration range of existence of mono- and dicationic forms of target porphyrin and corresponding ionization constants were evaluated.

5-Aza-2,3,7,8,12,13,17,18-octamethylporphyn was prepared in 69% yield by the reaction of 1,19-

dibromo-2,3,7,8,12,13,17,18-octamethylbiladiene *a,c*-dihydrobromide with sodium azide in DMF. The key 1,19-dibromo-2,3,7,8,12,13,17,18-octamethylbiladiene *a,c*-dihydrobromide was synthesized by condensation of 5,5'-dicarboxy-3,3',4,4'-tetramethyldipyrrolylmethane with two equivalents of 2-bromo-3,4-dimethyl-5-formylpyrrole under the action of hydrobromic acid in methanol.



To the acid–base interactions of azaporphyrins with acids the intracyclic (pyrrolenine) as well as the extracyclic (*meso*) nitrogen atoms can be involved. Therefore it is principally important to establish the number and the location of electron-donating reaction centers in the macroring. Ionization studies of the compound **V** in the ethanol–sulfuric acid mixtures by means of the spectrophotometric titration showed that protonation of tetrapyrrole macroring is accompanied by the consequent (depending on the acid concentration) formation of two sets of spectral curves. Each set has its own assembly of the isobestic points (Fig. 1).

The study of ionization of compound **V** in the 1×10^{-5}–3×10^{-4} M concentration range of sulfuric acid (related to the first set of spectral curves) showed the existence of one step on the corresponding titration curve. It is a strait line with the slope angle tangent close to unity (Fig. 2). That means that the acid-base interaction in the system of compounds **V**–C_2H_5OH–H^+ in the above-mentioned range of the sulfuric acid concentrations leads to formation of the mono-protonated form of the substance **V** and may be described by the Eq. (1). Further increase in the acid concentration leads to appearance of new set of

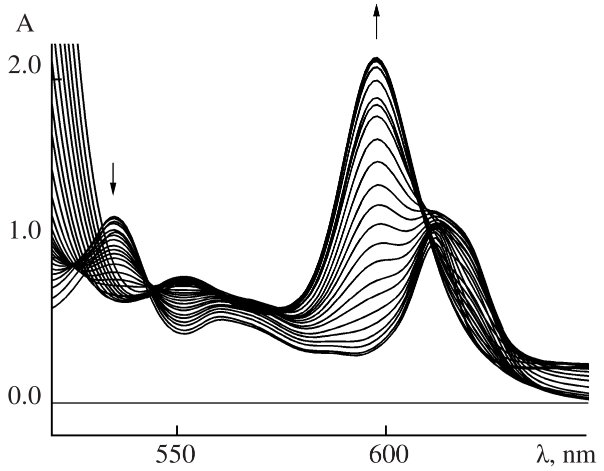


Fig. 1. Alterations in the electron absorption spectra of the **V**–C_2H_5OH–H_2SO_4 system [C_{porph} 1.81×10^{-5} M, $C(H_2SO_4)$ 1×10^{-5}–6×10^{-4} M].

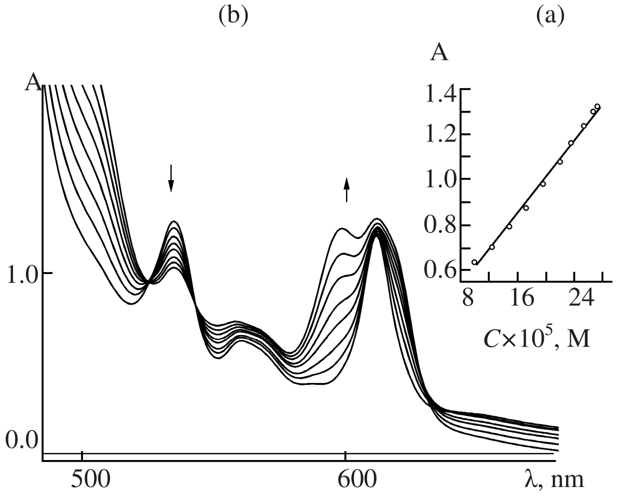


Fig. 2. (a) The curve of spectrophotometric titration of the product **V** (1.81×10^{-5} M) with sulfuric acid (1×10^{-5}–3×10^{-4} M) at the wavelength λ 598 nm (298 K). (b) Alterations in the electron absorption spectra of the **V**–C_2H_5OH–H_2SO_4 system [C_{porph} 1.81×10^{-5} M, $C(H_2SO_4)$ 1×10^{-5}–3×10^{-4} M].

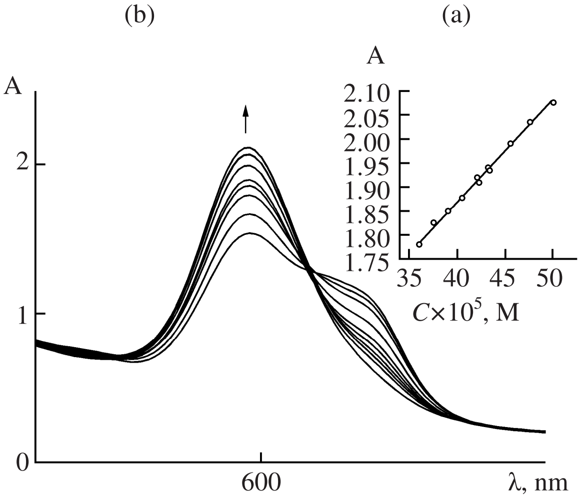


Fig. 3. (a) The curve of spectrophotometric titration of the product **V** (1.81×10^{-5} M) with sulfuric acid (3.21×10^{-4}–6×10^{-4} M) in ethanol at the wavelength λ = 598 nm (298 K). (b) Alterations in the electron absorption spectrum in the **V**–C_2H_5OH–H_2SO_4 system [C_{porph} 1.81×10^{-5} M, $C(H_2SO_4)$ 3.21×10^{-4}–6×10^{-4} M].

spectral curves forming another assembly with its own set of isobestic points (Fig. 3).

The presence of one step only on the corresponding titration curve of azaporphyrin in the acid concentration range 3.21×10^{-4}–6×10^{-4} M (corresponding to the second set of spectral curves) permits to describe the protonation of monoprotonated form of the macroring by the Eq. (2).

The transformation of the two-band electron absorption spectrum of moderate intensity [λ_{max} 535 nm (log ε 3.74), λ_{max} 612 nm (log ε 3.8)] to the one-band [λ_{max} 590 nm (log ε 4.07)] electron absorption spectrum of high intensity (Fig. 1) observed in the course of the macrocycle protonation according to the published data [11] and the results obtained by us [10] confirms that just the intracyclic nitrogen atoms are protonated. Hence, nitrogen atoms in the *meso*-positions of the macrocycle **V** do not take part in the acid-base interactions. The spectral changes established permit to calculate the corresponding stepwise ionization constants by means of the standard procedure [6, 10]. The constants of formation of the protonated forms H_3P^+ and H_4P^{2+} in the H_2P–C_2H_5OH–H_2SO_4 system [C_{porph} ~ 1.5×10^{-5}–1.8×10^{-5} M, $C(H_2SO_4)$ 2×10^{-6}–6×10^{-4} M] are the following:

Porphyrin	**V**	**VI**[1]
Kb_1	353	63
Kb_2	398	65

The values of ionization constants of the compounds **V** and **VI** and the concentration ranges of existence of their mono- and dicationic forms show that in the solution of sulfuric acid in ethanol the basic properties of the porphyrins **V** and **VI** are comparable. At the same time formation of the cations **V** is accompanied by the clear and easily identified responce in the visible range of the absorption spectrum (Fig. 4) that creates the conditions for more effective control of physicochemical processes taking place with the participation of tetrapyrrole chromophore as compared to the compound **VI**.

Thus, in the presented work mesomonoazaporphyrin **V** was synthesized and its basic properties were studied by means of spectrophotometric titration. Protonation of the intracyclic nitrogen atoms of the tetrapyrrole chromophore synthesized in the solution of sulfuric acid in ethanol is found proceeding in two

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[1] **VI** is 3,7,13,17-tetramethyl-2,8,12,18-tetrabutylporphyrin [6].

steps. The corresponding ionization constants and the concentration ranges of existence of tetrapyrrolic mono- and dications are evaluated. The data obtained show that application of the synthesized azaporphyrin as a key substance for creation of pH-switching molecular optical devices with the purpose of detecting and selective binding of anions in solutions is promising.

EXPERIMENTAL

^{1}H NMR spectra were taken on a Bruker VC-200 (200 MHz) spectrometer in $CDCl_3$ against internal TMS. Electron impact mass spectra were obtained on a MX-1310 spectrometric complex, the ionizing electron energy 70 eV, the ionization chamber temperature 150–200°C. Spectrophotometric titration of azaporphyrin with sulfuric acid in ethanol was carried out on a Varian Cary 100 spectrophotometer. Experimental procedure and treating of the data obtained are described in [6, 10]. The protonation constants were calculated according to the Eqs. (3) and (4).

$$\mathrm{p}k_{b1} = \mathrm{H}_0 + \log\,[C(\mathrm{H_3P^+})/C(\mathrm{H_2P})], \tag{3}$$

$$\mathrm{p}k_{b2} = \mathrm{H}_0 + \log\,[C(\mathrm{H_4P^{2+}})/C(\mathrm{H_3P^+})]. \tag{4}$$

The error of evaluation of the corresponding constants was 3–5%.

2-Formyl-5-bromo-3,4-dimethylpyrrole (II). To a solution of 6.8 g of 3,4-dimethylpyrrole **I** [8] in 40 ml of benzene and 20 ml of DMF 9 ml of benzoyl chloride was added with stirring and cooling. The mixture obtained was stirred for 1 h, the precipitate formed was filtered off, washed with benzene, dried and dissolved in 35 ml of acetic acid. The solution obtained was treated with 3.5 ml of bromine. The reaction mixture was stirred for 15 min, and then treated with a solution of 12 g of sodium acetate trihydrate in 100 ml of water and heated on a water bath for 0.5 h. The precipitate formed was filtered off, dried in air at room temperature and crystallized from methanol. Yield 9.9 g (68%). ^{1}H NMR spectrum ($CDCl_3$, HMDS), δ, ppm: 9.23 (1H, CHO); 2.17 s (3H, 3-CH_3), 1.83 s (3H, 4-CH_3).

5,5'-Dicarboxy-3,3',4,4'-tetramethyldipyrrolylmethane (III). A solution of 4.0 g of 5,5'-bis(ethoxycarbonyl)-3,3',4,4'-tetramethyldipyrrolylmethane [9] in 100 ml of ethanol was heated to boil and treated with a solution of 3.0 g of potassium hydroxide in 20 ml of water. The reaction mixture was refluxed for 4 h, ethanol was distilled off in a vacuum at room temperature, and the residue was diluted with 100 ml of water. The mixture obtained was filtered, the filtrate was acidified with the diluted hydrochloric acid, and the precipitate formed was filtered off, washed with water and dried on air at 30°C. Yield 3.3 g (98%).

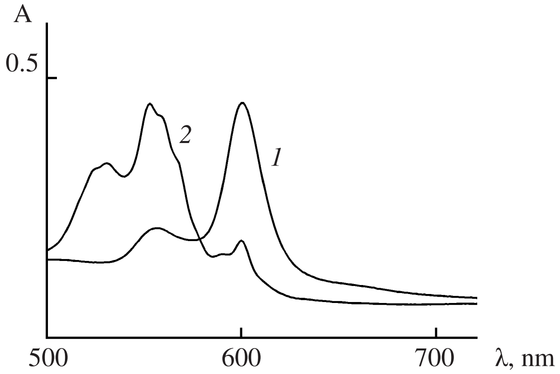

Fig. 4. The electron absorption spectrum of the compounds (*1*) **V** and (*2*) **VI** in the H_4P^2–C_2H_5OH–H_2SO_4 system [C_{porph} ~1.5×10^{-5}–1.8×10^{-5} M, $C(H_2SO_4)$ 1×10^{-4}–6×10^{-4} M] at 298 K.

1,19-Dibromo-2,3,7,8,12,13,17,18-octamethylbiladien-*a,c* dihydrobromide (IV). Pyrrole **II**, 0.7 g, and 0.5 g of dipyrrolylmethane **III** were dissolved in 20 ml of boiling methanol. A solution obtained was treated with 5 ml of concentrated hydrobromic acid, cooled, and kept for 12 h at 5°C. The precipitate formed was filtered off, washed consequently with cooled methanol and ether, and dried in air at room temperature. Yield 0.9 g (71%). Electron absorption spectrum, $\lambda_{\max}$, nm (log ε): 459 (4.83), 536 (5.06) (methylene chloride). The product was used without further purification.

5-Aza-2,3,7,7,12,13,17,18-octamethylporphyn (V). A mixture of 0.5 g of biladiene-*a,c* **IV**, 0.3 g of sodium azide, and 50 ml of DMF was boiled for 0.5 h. Then the reaction mixture was poured to 200 ml of water, the precipitate formed was filtered off, washed with water, and dried in air at 70°C. The product obtained was dissolved in a mixture of 1 ml of trifluoroacetic acid and 50 ml of chloroform, the solution obtained was filtered and treated with 2 ml of diethylamine. The precipitate formed was filtered off, washed with chloroform, and dried in air at 70°C. Yield 0.2 g (69%). The electron absorption spectrum, $\lambda_{\max}$, nm (log ε): 612 (4.18), 561 (3.80), 538 (4.20), 503 (3.81), 376 (4.95) (tetrachloroethane). Mass spectrum, *m/z* (I_{rel}, %): 424.55(77), [M + 1].

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