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Synthesis and Spectrophotometric Study of the Acid–Base and Complexing Properties of 2,3,7,8,12,13,17,18-Octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin in Acetonitrile

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Abstract—2,3,7,8,12,13,17,18-Octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin has been synthesized, and its acid–base and complexing properties in the systems 1,8-diazabicyclo[5.4.0]undec-7-ene–acetonitrile, acetonitrile–$Zn(OAc)_2$, and 1,8-diazabicyclo[5.4.0]undec-7-ene–acetonitrile–$Zn(OAc)_2$ have been studied by spectrophotometry. Titration of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin with 1,8-diazabicyclo[5.4.0]undec-7-ene is accompanied by successive deprotonation of the pyrrole nitrogen atoms with formation of the corresponding mono- and dianion. The overall acid dissociation constant of the title compound has been determined. The complexation of neutral and doubly deprotonated 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin with $Zn(OAc)_2$ has been studied, and kinetic parameters for the formation of the zinc complex according to the molecular and ionic mechanisms have been determined. Extra coordination of 1,8-diazabicyclo[5.4.0]undec-7-ene by the zinc complex of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin.

Keywords: porphyrin, metal complexes, kinetics, deprotonation

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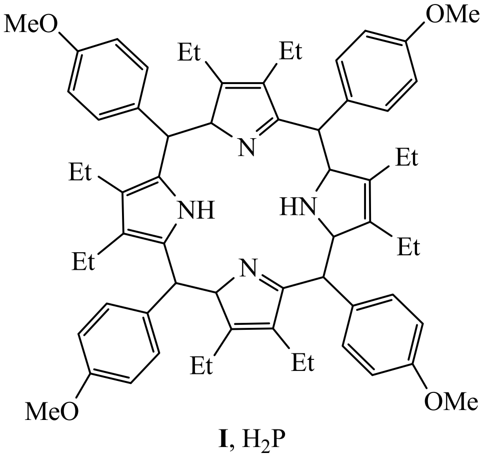
One of the most important problems of natural science is elucidation of mechanisms of action of tetrapyrrole compounds in natural systems with the goal of creating their artificial analogs [1–5]. Tetrapyrrole macrocycles, especially their metal complexes, play an exceptional role in the vital activity of humans and animals, which stimulates persistent interest in their synthesis and studies on the structure and properties of artificial analogs with the aid of various physicochemical methods [6–9].

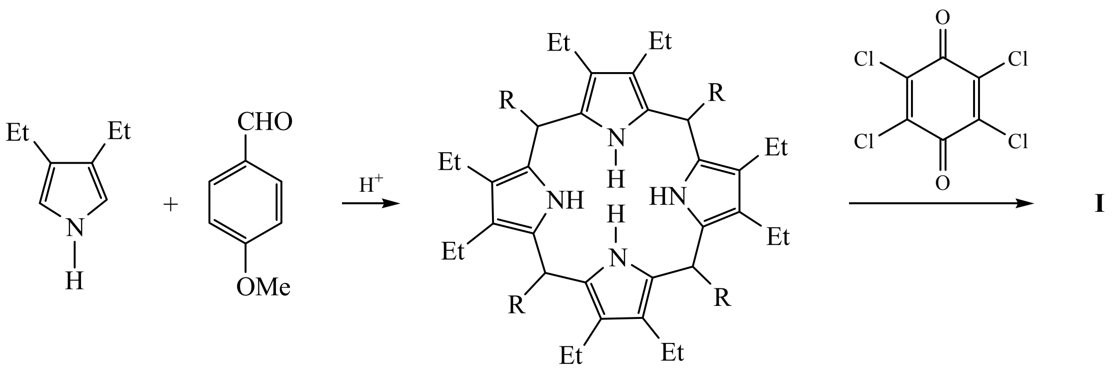
Complex formation of tetrapyrrole macrocycles with metal ions may follow two mechanisms: molecular mechanism involving neutral ligand and ionic mechanism with participation of deprotonated ligand [5, 10, 11, 12]. Both mechanisms occur in nature, and solvation often affects the rate of complex formation to a stronger extent than do electronic properties of the substituents [11, 12]. Comparison of these mechanisms with a view of finding optimal conditions for coordination of metal cation to tetrapyrrole ligand attracts considerable interest from the viewpoint of using the results in both industry and medicine [11–15]. For this purpose, we have synthesized 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-

Scheme 1.



I, H_2P

Scheme 2.



methoxyphenyl)porphyrin (**I**, H_2P) and studied by spectrophotometry its acid–base properties and complexing ability toward zinc(II) acetate in the systems 1,8-diazabicyclo[5.4.0]undec-7-ene–acetonitrile (**1**) (298 K), acetonitrile–$Zn(OAc)_2$ (**2**) (298–318 K), and 1,8-diazabicyclo[5.4.0]undec-7-ene–acetonitrile–$Zn(OAc)_2$ (298–318 K) (**3**) (Scheme 1).

Porphyrin **I** was obtained by condensation of 3,4-diethyl-1*H*-pyrrole with 4-methoxybenzaldehyde in methanol in the presence of hydrobromic acid, followed by oxidation of the porphyrinogen thus formed with *p*-chloranil according to a procedure analogous to that described in [16, 17] (Scheme 2).

The electronic absorption spectrum of porphyrin **I** was recorded in chloroform with addition of triethylamine to avoid protonation of macrocycle with trace of acid present in the solvent. The ^1H NMR spectrum of **I** was recorded in chloroform-*d* in the presence of trifluoroacetic acid.

Mutual transformations of different conformers of the neutral form would lead to the appearance in the ^1H NMR spectrum of broadened unresolved signals from protons in the ethyl and NH groups. In the presence of trifluoroacetic acid, the protonated porphyrin exists as a single conformer which displays a well resolved spectrum. Signals from magnetically nonequivalent

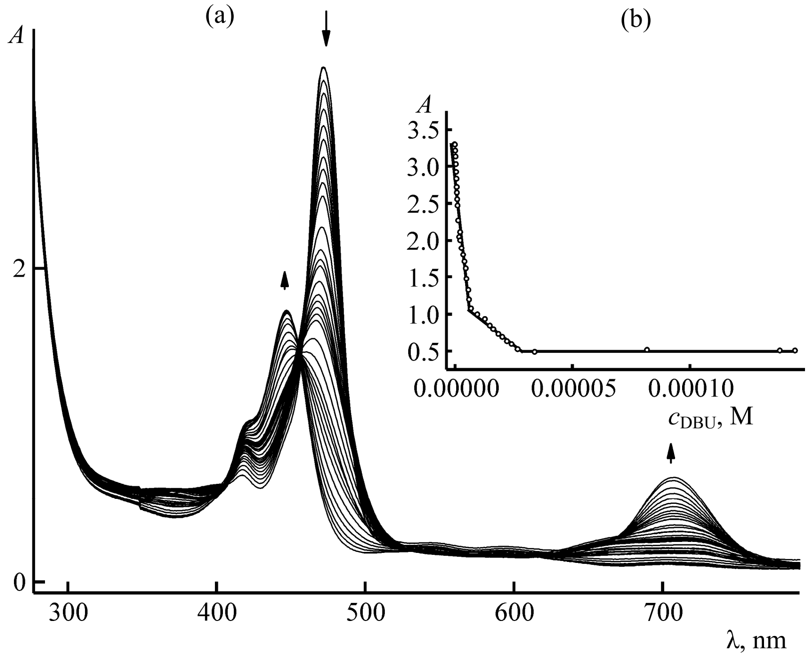


Fig. 1. (a) Variation of the electronic absorption spectra of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)-porphyrin (**I**) in acetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (system **1**, 298 K) and (b) spectrophotometric titration of porphyrin **I** in system **1** (λ 472 nm, $c_I = 7.5 \times 10^{-5}$ M, $c_{DBU} = 0–1.45 \times 10^{-4}$ M, 298 K).

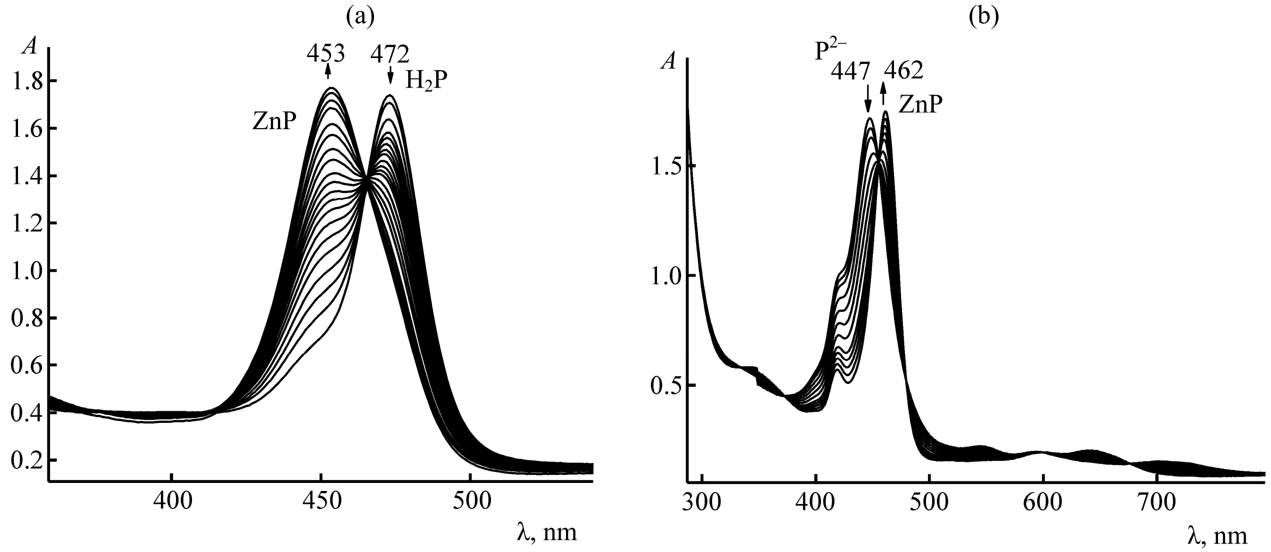


Fig. 2. Variation of the electronic absorption spectra in the course of coordination of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis-(4-methoxyphenyl)porphyrin (**I**) with zinc(II) acetate in acetonitrile at 298 K in systems (a) **2** and (b) **3**.

methylene protons in the ethyl groups appeared as two quartets.

Figure 1 shows variation of the electronic absorption spectrum of porphyrin **I** in acetonitrile during titration with a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). As the concentration of DBU increased, the spectra displayed two families of spectral curves, each being characterized by its own set of isosbestic points. The electronic absorption spectrum of porphyrin **I** as free base (molecular form) had the following parameters, λ_{max}, nm (logε): 417 sh, 472 (4.44), 708 (3.98). When the concentration of DBU attained 7.06×10^{-6} M, the spectral pattern corresponded to monoanion HP^-, λ_{max}, nm (log ε): 460 (4.32), 720 (3.49). Further raising the DBU concentration from 7.06×10^{-6} to 1.45×10^{-4} M led to the spectrum of dianion P^{2-} [λ_{max}, nm (logε): 447 (4.39), 544 (3.47), 594 (3.41), 702 (3.21)]. Analogous acid–base transformations of organic compounds in solution are well known [18–20].

On the basis of our experimental data, spectrophotometric titration curve was plotted (Fig. 1), which indicated that the reaction of H_2P with DBU in fact includes two steps (1) and (2).

$$H_2P \overset{k_1}{\rightleftarrows} HP^- + H^+, \qquad (1)$$

$$HP^- \overset{k_2}{\rightleftarrows} P^{2-} + H^+. \qquad (2)$$

Using Eq. (3) we calculated the overall acid ionization constant (K_a) for two steps. Its value for H_2P in the system 1,8-diazabicyclo[5.4.0]undec-7-ene–MeCN at 298 K was $\log K_a = \log(K_1K_2) = -11.04$ (±3–5%).

$$\log K_a = \log Ind + n \log c_{DBU}. \qquad (3)$$

Here, $Ind = c_{P2-}/c_I$ is the indicator ratio, c_{DBU} is the concentration of 1,8-diazabicyclo[5.4.0]undec-7-ene (M), and $n = 2$ is the number of protons abstracted by DBU.

With account taken of equilibria (1) and (2) and material balance equation (4) simple calculations [18] showed that at a DBU concentration of about 1.3×10^{-4} M almost all porphyrin **I** molecules exist as dianions.

$$c_0 = c_I + c_{P2-}. \qquad (4)$$

The kinetics of the formation of zinc complexes of porphyrin **I** were studied by spectrophotometry in systems **2** and **3** (Fig. 2). The formation of porphyrin complexes with doubly charged metal cations in nonaqueous solution may be described by Eqs. (5) and (6).

$$H_2P + [MX_2(Solv)_{n-2}] \rightarrow MP + 2HX + (n-2)Solv, \qquad (5)$$

$$P^{2-} + [MX_2(Solv)_{n-2}] \rightarrow MP + 2X^- + (n-2)Solv. \qquad (6)$$

Here, X is an anionic ligand, Solv is a solvent molecule, and n is the coordination number of metal cation.

The kinetic parameters were calculated according to standard procedure using Eqs. (7)–(12).

$$k_{ef} = (1/\tau)\ln(c^0_I/c_I). \qquad (7)$$

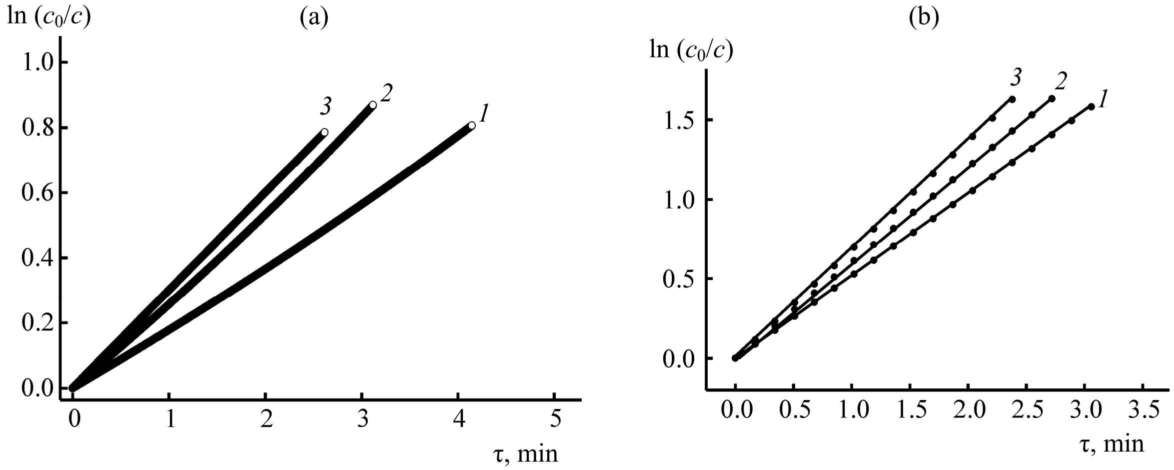


Fig. 3. Plots of log (c_0/c) versus time τ for the complex formation of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin (**I**) with zinc(II) acetate in systems (a) **2** $\{c_\mathrm{I} = 5.60 \times 10^{-5}$ M, $[\mathrm{Zn(AcO)_2}] = 5.60 \times 10^{-3}$ M$\}$ and (b) **3** $\{c_\mathrm{I} = 4.71 \times 10^{-5}$ M, $[\mathrm{Zn(AcO)_2}] = 4.71 \times 10^{-4}$ M$\}$ at (*1*) 298, (*2*) 308, and (*3*) 318 K.

Taking into account variation of the optical density, we obtain Eq. (8):

$$k_\mathrm{ef} = (1/\tau)\ln[(A_0 - A_\infty)/(A_\tau - A_\infty)], \tag{8}$$

where τ is the time elapsed from the reaction start, and A_0, A_τ, and A_∞ are the optical densities of the reaction solution at the initial moment, moment τ, and by the end of the reaction, respectively. The true rate constant was calculated by formula (9):

$$k_{n+1} = k_\mathrm{ef}/c^n_\mathrm{salt}. \tag{9}$$

Here, k_{n+1} is the $(n + 1)$-order rate constant.

The energy of activation was calculated by the Arrhenius equation on the basis of the temperature dependence of the rate constant.

$$k = Ae^{-E_\mathrm{a}/RT}, \tag{10}$$

$$E_\mathrm{a} = 19.1[T_1T_2/(T_2 - T_1)]\log(k_2/k_1). \tag{11}$$

The entropy of activation $\Delta S^{\neq}$ was determined using Eq. (12):

$$\Delta S^{\neq} = 19.1\ln k^{298} + E_\mathrm{a}/298 - 253. \tag{12}$$

Kinetic experiments were carried out at least in triplicate at each temperature. The order of the reaction with respect to porphyrin was determined from the linear dependence of log $(c^0_\mathrm{I}/c_\mathrm{I})$ versus time ($n = 1$, Fig. 3). The order of the reaction with respect to the metal salt was determined graphically as the slope of the linear plot of log k_ef vs. –log $[\mathrm{Zn(OAc)_2}]$ (Fig. 4). The kinetic parameters for the formation of porphyrin zinc complexes are given below.

System	$[\mathrm{Zn(OAc)_2}]$, M	k^{298}, L mol^{-1} s^{-1}	E_a, kJ/mol	$\Delta S^{\neq}$, J mol^{-1} K^{-1}
2 ($\mathrm{H_2P}$)	5.60×10^{-3}	0.53 ± 0.02	22 ± 4	–34 ± 1
3 ($\mathrm{P^{2-}}$)	4.71×10^{-4}	18.19 ± 0.09	12 ± 2	–2.2 ± 0.3

The zinc complexes of porphyrin **I** formed in systems **2** and **3** essentially differed from each other in the position of bands in the electronic absorption spectra (Figs. 2a, 2b). We presumed that 1,8-diazabicyclo[5.4.0]undec-7-ene, as well as other nitrogen bases (pyridine, piperidine, imidazole, etc.) is capable of coordinating as extra ligand to the central metal ion of the porphyrin complex. Porphyrin metal complexes with extra ligands are characterized by a red shift of absorption bands in the electronic spectra, whose value depends on the strength of the dative bond between the extra ligand and metal ion [19]. In order to verify the above assumption we recorded the electronic absorption spectra of ZnP in a coordinating (acetonitrile) and noncoordinating solvent (toluene), as well as with addition of liganding co-solvents (Figs. 5a, 5b).

During the reaction with zinc acetate in system **2** [reaction (5)] the electronic absorption spectrum of neutral ligand **I** gradually transformed into the spectrum of complex ZnP [λ_max, nm (log ε): 453 (4.30), 593 (3.25), 646 (3.22)] (Figs. 2a, 5a). Subsequent addition of DBU to the resulting solution of complex ZnP in acetonitrile induced a red shift of the absorption

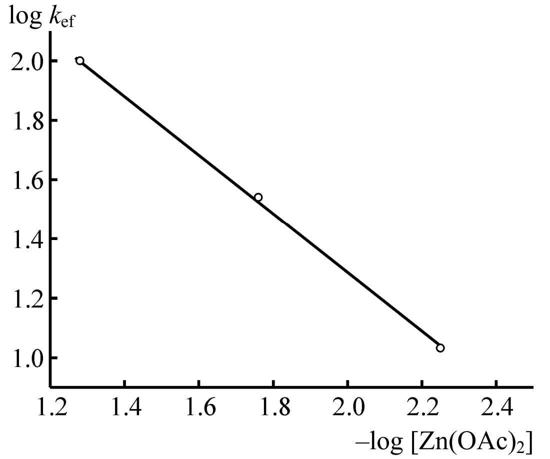


Fig. 4. Plot of logk_{ef} versus –log [Zn(OAc)$_2$] for the reaction of 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin (**I**) with zinc(II) acetate in acetonitrile at 298 K (tan α = 1.02, $r = 0.999$).

bands approximately by 7–10 nm, presumably, due to extra coordination of DBU [λ_{max}, nm (logε): 462 (4.30), 600 (3.29), 656 (3.29)]. In the reaction of Zn (OAc)-$_2$ with doubly deprotonated ligand P^{2-} [system **3**, reaction (6)], the electronic absorption spectrum of the resulting complex had the same parameters. The electronic absorption spectra of specially synthesized zinc complex of porphyrin **I** in acetonitrile and toluene were analogous to the spectrum of the titration product in system **3** (Figs. 5a, 5b), but the bands in the spectra of the former were displaced blue. Addition of pyridine to a solution of ZnP in toluene leads to a red shift of the absorption bands whose maxima almost coincide with those observed in system **3** (Fig. 5b). The electronic absorption spectrum of ZnP in toluene (noncoordinating solvent) slightly differs from the spectrum in acetonitrile (Figs. 5a, 5b). Obviously, there is no extra coordination in toluene. When pyridine is added to a toluene solution of ZnP (or DBU is added to a solution ZnP in acetonitrile), coordination of extra ligand is likely to produce complexes with a definite stoichiometry, which leads to a red shift of absorption bands in the electronic spectra.

In summary, our kinetic study on the complexing properties of neutral 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin (**I**) and its dianion toward zinc acetate in acetonitrile showed that the complexation with the latter is characterized by a considerably higher rate and lower energy of activation E_a (approximately by half). Obviously, this is determined by lower energy expenditure for deformation of the macrocycle and dissociation of the N–H bonds, and decrease of $\Delta S^{\neq}$ indicates more ordered transition state. The rate of formation of zinc complex ZnP according to the molecular mechanism [reaction (5), system (**2**)] is lower by a factor of 34 than in system **3** [ionic mechanism (6)]. Our results may be useful in the design of reaction systems involving complex formation processes, as well as of molecular devices

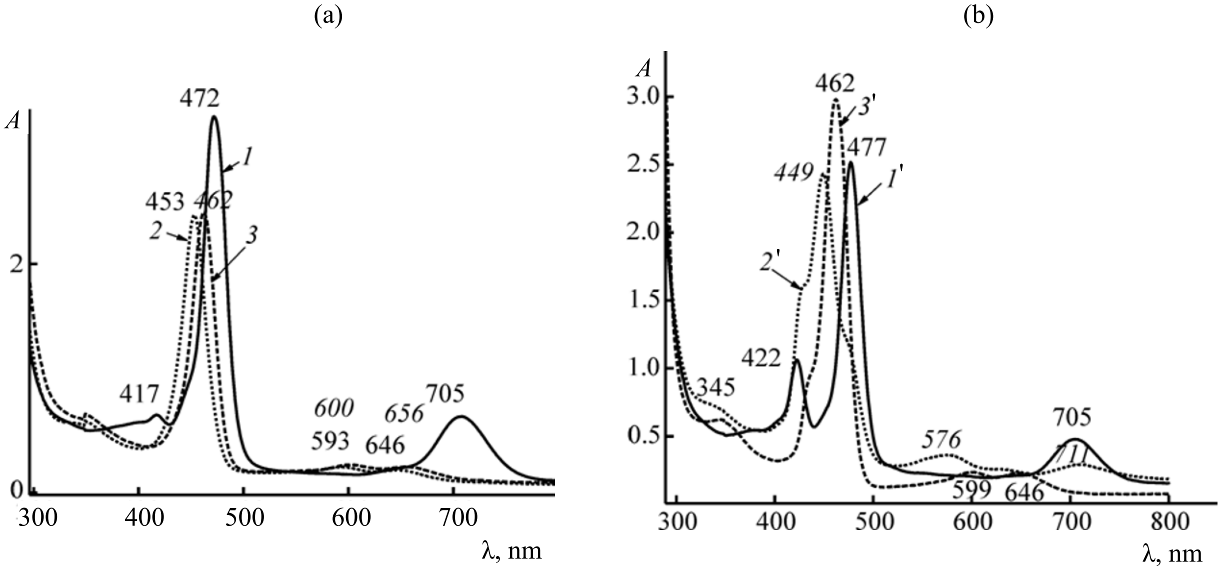


Fig. 5. Electronic absorption spectra in (a) acetonitrile and (b) toluene of (*1*, *1'*) 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(4-methoxyphenyl)porphyrin (**I**), (*2*, *2'*) zinc complex ZnP, and zinc complex ZnP with addition of (*3*) 1,8-diazabicyclo[5.4.0]undec-7-ene and (*3'*) pyridine.

with specified properties, in particular for binding metal ions in organic media.

EXPERIMENTAL

Spectrophotometric titration of a solution of porphyrin **I** in acetonitrile with 1,8-diazabicyclo[5.4.0]-undec-7-ene was carried out using a Varian Cary 100 spectrophotometer. The experimental and data treatment procedures were described in [20, 21]. The error in the determination of the acidity constants was ±3–5%. The electronic absorption spectra were recorded on Shimadzu UV-1800, Hitachi U-2000, and Varian Cary 100 spectrophotometers. The ^{1}H NMR spectrum of porphyrin **I** was measured in $CDCl_3$ on a Bruker AV III-500 spectrometer at 500 MHz using tetramethylsilane as internal reference.

Ultrapure acetonitrile (water content <0.03%) and 1,8-diazabicyclo[5.4.0]undec-7-ene with pK_a 13.2 in acetonitrile were used. Zinc(II) acetate of analytical grade was purified by recrystallization from aqueous acetic acid and was dried at 380–390 K [22].

2,3,7,8,12,13,17,18-Octaethyl-5,10,15,20-tetrakis-(4-methoxyphenyl)porphyrin (I). Concentrated aqueous HBr, 2.0 mL (~17 mmol), was added under stirring in an argon atmosphere to a solution of 1.0 g (8.12 mmol) of 3,4-diethyl-1*H*-pyrrole and 0.82 mL (8.12 mmol) of 4-methoxybenzaldehyde in 50 mL of methanol. The mixture was stirred for 4 h at room temperature, and the precipitate of porphyrinogen was filtered off, washed with methanol, and (without drying) dissolved in 40 mL of THF. A suspension of 1.4 g (5.7 mmol) of *p*-chloroanil in 30 mL of THF was added to the solution, and the mixture was stirred for 5 h at room temperature. The solvent was distilled off, and the residue was washed with a 5% solution of sodium hydroxide and water and dried in air at 70°C. The product was dissolved in methylene chloride and subjected to chromatography on aluminum oxide (activity grade III) using chloroform as eluent. The green zone was eluted, the eluate was evaporated to a minimum volume, and porphyrin **I** was precipitated with methanol, filtered off, washed with methanol, and dried in air at 20°C. Yield 0.84 g (43%), R_f 0.30 (Silufol, benzene–methanol, 1:1). Electronic absorption spectrum ($CHCl_3$ + 0.5% Et_3N), λ_{max}, nm (logε): 703 (3.96), 603 (4.05), 552 (4.08), 454 (5.32). ^{1}H NMR spectrum ($CDCl_3$ + 1% CF_3COOH), δ, ppm: 8.18 d (8H, 2′-H, 6′-H, J = 8.1 Hz), 7.78 d (8H, 3′-H, 5′-H, J = 8.1 Hz), 4.13 s (12H, OCH_3), 2.44 q and 2.18 q (8H each, $C\mathbf{H}_2CH_3$, J = 7.6 Hz), 0.20 t (24H, $CH_2C\mathbf{H}_3$, J = 7.6 Hz), –0.19 br.s (4H, NH).

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