## Influence of Substituents Structure and Their Electronic Effects on Acid-Base and Complexing Properties of 5,10,15,20-Tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin

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**Abstract**—5,10,15,20-Tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin has been prepared, and its acid-basic properties have been studied in acetonitrile by titration with 1,8-diazabicyclo [5.4.0]undec-7-ene and perchloric acid. The substituted porphyrin ability towards complex formation with zinc acetate has been studied in acetonitrile and acetonitrile, 1,8-diazabicyclo [5.4.0]undec-7-ene media. Spectral properties of neutral and ionic forms of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin and its zinc complex have been determined; constants of acid and basic ionization of the ligand have been estimated. Kinetic parameters of the porphyrin complex formation with zinc via molecular and ionic mechanism have been analyzed. The substituents effect on the studied properties is discussed.

Keywords: porphyrin, metal complex, complexation kinetics, deprotonation

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In natural hemoproteins, enzymatic activity of metal porphyrins occurs via coordination of additional ligands and is balanced by conformational changes in the macrocycle due to its hydrophilic or hydrophobic surrounding [1-3]. The deformation of tetrapyrrole macrocycle is among the most efficient ways of regulation of coordination ability and other physicochemical properties of porphyrins and related macrocycles [4–9]. Non-planarity of porphyrin macrocycle can arise from a number of factors, including modification with bulky substituents [4]. Deformation of the tetrapyrrole scaffold significantly affects the acid-basic properties of the porphyrin ligand [10, 11] and may either accelerate (in basic solvents) or slow down (in acidic solvents) the complex formation by several orders of magnitude [4, 12, 13]. Moreover, a substituent itself, being either donor of acceptor of electrons, can affect acid-basic properties of porphyrins and their complex formation ability.

We have reported on electron and spatial effects of porphyrin substituents on their acid-base and complex formation properties elsewhere [11–14]. Developing these studies, herein we have evaluated acid and basic ionization constants of 2,3,7,8,12,13,17,18-octaethylporphyrin I and 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18octaethylporphyrin II as well as kinetics of their complexes formation with zinc; the latter macrocycle contains strong electron acceptors in the *meso*positions of the macrocycle.

Acid-base properties of porphyrins I and II were studied by spectrophotometric titration in the acetonitrile–perchloric acid and acetonitrile–1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) mixtures at 298 K as described elsewhere [15]. Accuracy of determination of the corresponding constants was within 3–5%.

Rate of formation of complexes of porphyrins I and II with zinc was measured by means of spectrophotometry in the constant-temperature cell at 298– 318 K ( $\pm 0.1$  K). Isosbestic points were clearly revealed in the spectra (Fig. 1).

Formation of the complex between porphyrin and metal cation in organic medium can be described by Eq. (1):

 $H_2P + [MX_2(Solv)_{n-2}] \rightarrow MP + 2HX + (n-2)Solv, (1)$ 





where X, acidic ligand; Solv, solvent molecule; and n, the metal cation coordination number. Generally, reaction (1) follows the first-order kinetics with respect to porphyrin [Eq. (2)] [16], see Fig. 2.

$$-dc(\mathrm{H}_{2}\mathrm{P})/dt = kc(\mathrm{H}_{2}\mathrm{P})c^{n}(\mathrm{M}\mathrm{X}_{2}).$$
(2)

In Eq. (2), k is the reaction rate constant,  $c^n(MX_2)$  is the salt concentration, and  $c(H_2P)$  is the porphyrin concentration. In this work, kinetic measurements were performed at 100-fold excess of the salt,  $Zn(OAc)_2$ , with respect to porphyrin; therefore, the effective rate constants  $k_{ef}$  of the complex formation could be determined by Eq. (3).

$$k_{\rm ef} = (1/t) \ln \left[ (A_0 - A_\infty) / (A - A_\infty) \right].$$
(3)



Fig. 1. Changes of electronic absorption spectrum upon coordination of dianion of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin with zinc acetate in CH<sub>3</sub>CN at 298 K.

In Eq. (3),  $A_0$ , A,  $A_\infty$  are the solution absorbances at the initial point, at time *t*, and after the reaction is complete, respectively.

The rate constants of (n + 1)-order were calculated using Eq. (4).

$$k_{n+1} = k_{\rm ef}/c^n [\rm Zn(OAc)_2].$$
<sup>(4)</sup>

The reaction rate order with respect to the salt was determined by measuring the effective reaction (1) rate constant as function of the salt concentration. In the studied case, the reaction rate order with respect to zinc acetate was equal to unity (acetonitrile solution), as seen from the plots of log  $[(A_0 - A_\infty)/(A - A_\infty)]$  vs. log *c* (Fig. 3).



**Fig. 2.** Kinetics of ln  $(c_0/c_i)$  change in the course of formation of zinc complex with 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin in CH<sub>3</sub>CN at: 298 K (1), 308 K (2), and 318 K (3)  $(c_{porph} 2.34 \times 10^{-5} \text{ mol/L}, [Zn(OAc)_2] 2.35 \times 10^{-3} \text{ mol/L}).$ 

Kinetic parameters of porphyrins I and II complexation with zinc ions are collected in Table 1.

From the published data [12, 13, 15, 17] it follows that the presence of four nitro groups in meso-positions if octaalkylporphyrin macrocycle leads to significant deformation of the porphyrin geometry, reflected in electronic absorption spectra. In particular, introduction of strong electron acceptors at the mesopositions leads to blue shift of the absorption bands. According to the four-orbital model (Simpson-Platt-Gouterman) [18], the blue shift is due to decreasing the energy of  $a_{2\mu}$  molecular orbital (HOMO) due to higher electron density at methine carbon atoms. However, red shift of all the absorption bands was observed in the spectrum of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18octaethylporphyrin as compared to that of planar analog I (Table 2). Evidently, of the simultaneously acting factors (deformation of the porphyrin scaffold, negative induction effect, and negative conjugation effect), the structural one played the decisive part.

The opposite contributions of structural and electronic effects of the substituents were in agreement with kinetic features of the complex formation reaction of porphyrins I and II (Table 1). As compared with the planar analogs, basicity of the distorted *meso*-phenyl-substituted octaalkylporphyrins is enhanced due to decreasing of their aromaticity and isolation of  $\pi$ -electron systems of the pyrrole and pyrrolein frag-



**Fig. 3.** log  $k_{ef}$  as function of log  $c[Zn(OAc)_2]$  in the case of zinc complex with porphyrin II in CH<sub>3</sub>CN at 298 K (tan  $\alpha$  1.2, correlation coefficient 0.9998).

ments [4]. This leads to accelerating of the complexes formation by several orders of magnitude (in neutral or basic solvents) [4]. Introduction of strong electron accepting substituents (NO<sub>2</sub>) weakens the N–H bond at the reactive site and should therefore accelerate reaction (1). At the same time, electron-accepting groups decrease the electron density at tertiary nitrogen atoms that does not favor strengthening of the N $\rightarrow$ M bonds of the intermediate state and should

**Table 1.** Parameters of electronic absorption spectra of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin in the CH<sub>3</sub>CN –DBU and CH<sub>3</sub>CN–Zn(OAc)<sub>2</sub> systems at 298 K

Form	$\lambda_1(\log \epsilon), nm$	$\lambda_2(\log \epsilon), nm$	$\lambda_3(\log \epsilon)$ , nm
H <sub>2</sub> P	434(4.76)	527(4.13)	615(3.76)
$\mathbf{P}^{2-}$	_	532(4.68)	683(3.88)
$H_4P^{2+}$	460(5.21)	607(4.27)	666(4.09)
ZnP	447(4.77)	579(3.98)	_

Table 2. Kinetic parameters of reaction of porphyrins coordination by zinc acetate in CH<sub>3</sub>CN and in CH<sub>3</sub>CN–DBU

Porphyrin	[Zn(OAc) <sub>2</sub> ], mol/L	$k^{298}$ , L mol s <sup>-1</sup>	$\Delta E$ , kJ/mol	$\Delta S^{\neq}$ , J mol <sup>-1</sup> K <sup>-1</sup>
I	$2.56  imes 10^{-3}$	64±2	47±4	-15±1
II	$2.35 \times 10^{-3}$	81±3	54±5	12±1
IIa	$2.73  imes 10^{-3}$	1103±9	4±0.4	-104±9



**Fig. 4.** Changes of electronic absorption spectra of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin ( $c_{porph}$  2.21 × 10<sup>-5</sup> mol/L) (a) and 2,3,7,8,12,13,17,18-octaethylporphyrin ( $c_{porph}$  1.25 × 10<sup>-4</sup> mol/L) (b) in the course of titration with CH<sub>3</sub>CN–HClO<sub>4</sub> (0–1.4 × 10<sup>-4</sup> mol/L) at 298 K; titration curves are shown as insets.

therefore decrease the rate of metal complex formation [16]. The latter effect results in moderate increase of the rate of (1) in the case of nitro derivative II as compared to the reference porphyrin I: the rates ratio was of 1.3 only (Table 1).

Certain relationship between acid-base and complexing properties of free porphyrins reflects the fact that the ligand protonation competes with the coordination reaction in proton-donor solvents. However, formation of the anionic forms of porphyrin accelerated the complex formation.

(De)protonation of the transannular nitrogen atoms of tetrapyrrole macrocycle can be represented by Eqs. (5)-(8).

$$H_2 P \rightleftharpoons HP^- + H^+, \qquad (5)$$

$$H_2 P^- \rightleftharpoons P^{2-} + H^+, \qquad (6)$$

$$H_2P + H^+ \rightleftharpoons H_3P^+, \qquad (7)$$

$$H_3P^+ + H^+ \stackrel{\text{def}}{\rightleftharpoons} H_4P^{2+}.$$
 (8)

In the equations above,  $H_2P$ ,  $HP^-$ ,  $P^{2-}$ ,  $H_3P^+$ , and  $H_4P^{2+}$  are neutral, deprotonated, and protonated porphyrin forms, respectively.

In the course of titration of the ligands (I or II) with perchloric acid, the electronic absorption spectrum of the neutral form was smoothly transformed into that of dication:  $H_4P^{2+-}(I)$ ,  $\lambda_{max}$ , nm (log  $\varepsilon$ ) 514 br (3.17), 548 (3.90), 590 (3.46); (II),  $\lambda_{max}$ , nm (log  $\varepsilon$ ) 460 (5.21), 607 (4.27), 666 (4.09). In the both cases, spectrophotometric titration curves ( $\lambda$  546 nm and  $\lambda$  460 nm) were step; taking into account the presence of two families of isosbestic curves, that evidenced about 2 stages of protonation (Figs. 4a, 4b). Electronic effect of the substituents in the macrocycle was one of the factors allowing spectral observation of the monocations. Generally, the stepwise protonation of porphyrins is observed when the electron density at nitrogen atoms is significantly different, and the stronger polarization of the molecule favors differentiation of the cation forms of the porphyrin.

The combined constant of the both stages of basic ionization was calculated using Eq. (9).

$$\log K_{\rm b} = \log Ind - 2\log c({\rm HClO_4}), \tag{9}$$

where  $K_{b}$ , the combined basicity constant; *Ind*, the indicator ratio,  $[H_4P^{2^+}]/[H_2P]$ ;  $c(HClO_4)$ ,concentration of perchloric acid in the system, mol/L. The combined basicity constants were of  $pK_b$  9.56 (I) and 11.85 (II) in the CH<sub>3</sub>CN–HClO<sub>4</sub> at 298 K. Thus, the basicity of tetranitro derivative was somewhat higher, due to the combined action of the steric factor and the electronic effects of the substituents.

Acid properties of the porphyrins under study were investigated using DBU as deprotonating agent. Similar interactions were discussed elsewhere [19–21].



**Fig. 5.** Changes of electronic absorption spectra of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin ( $c_{porph}$  4.83 × 10<sup>-5</sup> mol/L) (a) and spectrophotometric titration curve ( $\lambda = 434$  nm) (b) in CH<sub>3</sub>CN–DBU (0–1.12 × 10<sup>-4</sup> mol/L) at 298 K.

An important advantage of organic base as deprotonating agent as compared to alkali is its solubility in organic media.

Similarly to the above-described protonation process, deprotonation of the porphyrin **II** resulted in two families of spectral curves, each corresponding to its own system of isosbestic points (Fig. 5). With increasing concentration of DBU from 0 to  $1.12 \times 10^{-4}$  mol/L, absorption spectrum of the neutral ligand was



Fig. 6. Current concentration of molecular and twice deprotonated forms of 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin in CH<sub>3</sub>CN–DBU (0–6.5 ×  $10^{-5}$  mol/L) at 298 K.

smoothly transformed into that of the dianion form (Table 1). The spectrophotometric titration curve ( $\lambda$  = 434 nm) was smooth and monotonous (Fig. 5). Taking into account the presence of two isosbestic points, that evidenced about close values of stepwise deprotonation constants [22]. Combined constant corresponding to the both stages of acid ionization was calculated using Eq. (10):

$$\log K_{\rm a} = \log Ind + 2\log c_{\rm DBU},\tag{10}$$



Fig. 7. Electronic absorption spectra of zinc complex with 5,10,15,20-tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin in CH<sub>3</sub>CN (*1*) and in CH<sub>3</sub>CN–DBU (*2*); and of the complex formed via interaction of dication of **IIa** with Zn(OAc)<sub>2</sub> in CH<sub>3</sub>CN–DBU (*3*).

where  $K_{\rm a}$ , the combined acidity constant; *Ind*, the indicator ratio,  $[{\rm P}^{2-}]/[{\rm H}_2{\rm P}]$ ;  $c_{\rm DBU}$ , concentration of DBU in the system, mol/L. The combined acidity constant of **II** equaled  $pK_{\rm a}$  10.44 in CH<sub>3</sub>CN–DBU at 298 K. The current concentrations of deprotonated and neutral forms of **II** were calculated accounting for the material balance equation; at  $c_{\rm DBU} \approx 6.5 \times 10^{-5}$  mol/L the porphyrin **II** was almost completely converted into the doubly deprotonated form (Fig. 6).

In the course of spectrophotometric titration of the porphyrin I with the organic base, spectra of the anionic forms were not detected at 298 K and at elevated temperature. Thus, I was much less acidic than II.

Coordination of porphyrins with salts of transition metals can occur either via molecular or via ionic route [17]. Formation of complexes of the porphyrin **II** with zinc ions was studied in the CH<sub>3</sub>CN–DBU–Zn(OAc)<sub>2</sub> system at 100-fold excess of the salt with respect to the porphyrin. The data collected in Table 2 revealed acceleration of the reaction by more than an order of magnitude when the neutral ligand **II** was transformed into the ionic form **IIa**. Simultaneously, the activation energy was down by 50 kJ/mol, and the activation entropy was down by 120 J mol<sup>-1</sup> K<sup>-1</sup>. That could be due to no energy losses upon deformation and cleavage of the N–H bonds of the reactive site as well as higher polarization of the molecule leading to more solvated state of the anionic form in the transition state.

NMR spectrum of the formed zinc complex completely coincided that of the compound prepared via reaction (1). However, the red shift (about 10 nm) of all absorption bands in the electronic spectra was revealed, due to additional coordination of the base present in the solution with the complex (Fig. 7).

## **EXPERIMENTAL**

Zinc acetate (*analytical pure* grade) was recrystallized from aqueous acetic acid and dehydrated at 380–390 K [23].

IR spectra were recorded using the Avatar 360 FTTIR ESP spectrometer (KBr). <sup>1</sup>H NMR spectra of solutions in CDCl<sub>3</sub> were recorded using the Bruker-500 spectrometer (500 MHz, TMS as internal reference). Electronic absorption spectra were recorded using the Shimadzu UVV1800 and Hitachi UU2000 Cary 100 Varian spectrophotometers.

1,8-Diazabicyclo[5.4.0]undec-7-ene (*special pure* grade) was used as received. Ionization constant of its

conjugated acid was of  $pK_a$  13.2 in acetonitrile [24]. The solvents (benzene, dichloromethane, perchloric acid, and acetonitrile) were purified as described elsewhere [25].

**5,10,15,20-Tetranitro-2,3,7,8,12,13,17,18-octaethylporphyrin (I)** was prepared as described in [26]. It was then purified via chromatography on Al<sub>2</sub>O<sub>3</sub> (Brockmann grade III) with dichloromethane as eluent. The product purity was monitored by TLC at Silufol plates (0.5 mm, Merck, CH<sub>2</sub>Cl<sub>2</sub> as eluent). Yield 60%. IR spectrum, cm<sup>-1</sup>: 1533 [ $\delta_{as}$ (NO<sub>2</sub>)], 1370 [ $\delta_{s}$ (NO<sub>2</sub>)]. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 3.49 (16H), 1.43 (24H). Electronic absorption spectrum (CH<sub>2</sub>Cl<sub>2</sub>),  $\lambda_{max}$ , nm (log  $\epsilon$ ): 426 (4.82), 530 (3.96), 572 sh (3.57), 611 (3.57), 665 (3.03).

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