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Synthesis and Spectrophotometric Study of Deprotonation of Octamethylporphyrin Derivatives with 1,8-Diazabicyclo[5.4.0]undec-7-ene in Acetonitrile

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Abstract—Acidic properties of synthesized 5,10,15,20-tetrakis(4'-*tert*-butylphenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin and 5,10,15,20-tetrakis(3',5'-di-*tert*-butylphenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin have been studied by spectrophotometry. Deprotonation of the intracyclic nitrogen atoms with 1.8-diazabicyclo [5.4.0]undec-7-ene in acetonitrile occurs in two steps. Deprotonation constants and ranges of the porphyrins-anionic forms existence have been determined, and influence of the peripheral substituents on acidic properties of the macrocyclic ligand has been elucidated.

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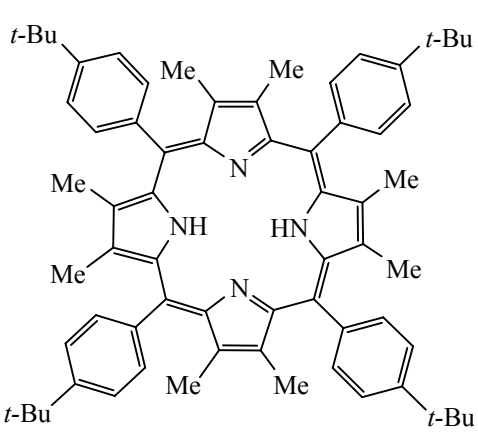
Natural porphyrins are known for a variety of biological functions, including oxygen transport and storage, light energy conversion into chemical one, electron transfer, catalysis, redox reactions, etc. [1–4]. In most of the natural objects (vitamin B_{12}-dependent enzymes, hemoproteins, methyl reductase, photosynthetic reaction center of bacteria, and others) the porphyrin molecules are non-planar, and degree of the macrocycle distortion changes depending on the molecule environment, spin state of the central ion, and nature of the axial ligands. In view of the recent data on porphyrins structure in enzyme systems, investigation of the effect of porphyrins macrocycle distortion on their reactivity is definitely a topical issue.

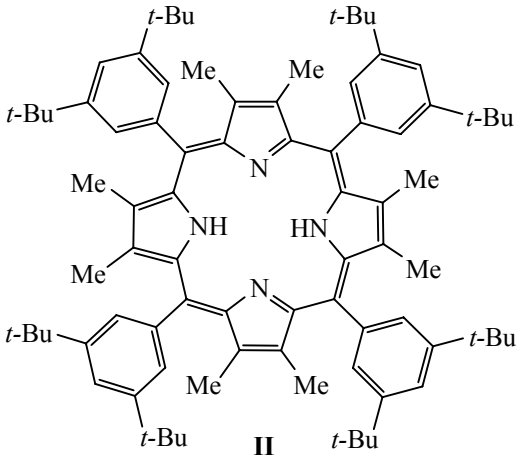
As shown previously [5–7], deformation of the planar structure of the porphyrin macrocycle generally reduces the molecule aromaticity and leads to somewhat more isolated pyrrole and pyrrolenine fragments, thus enhancing either basic [6] or acidic properties [7] of the macrocycle. Seemingly, porphyrins with the distorted macrocycle structure should be easily deprotonated in the presence of organic bases and, therefore, the metalloporphyrins formation should be accelerated. This work extended the study of acidic properties of the functionalized porphyrins [8, 9].

The octamethylporphyrin derivatives: 5,10,15,20-tetrakis(4'-*ter*t-butylphenyl)-2,3,7,8,12,13,17,18-octamethylporphin (**I**) and 5,10,15,20-tetrakis(3'5'-di-*tert*-butylphenyl)-2,3,7,8,12,13,17,18-octamethylporphin (**II**) were prepared, and their acidic properties were studied by spectrophotometric titration with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile at 298 K (see Scheme 1).

The changes of electron absorption spectra in the course of spectrophotometric titration of **I** and **II** with DBU in acetonitrile are documented in Figs. 1 and 2, respectively. Analysis of the absorbance curves (see inserts in Figs. 1 and 2) revealed that deprotonation of the intracyclic nitrogen atoms of **I** and **II** occurred in two steps. With increasing DBU concentration, the two series of bands were enhanced in the electron absorption spectra, and the corresponding set of isosbestic points was observed. The compounds concentrations were determined using the known molar absorption coefficients. The experimental electron absorption spectra parameters are summarized in the table.

Scheme 1.





The scheme of the titration reactions in the studied solutions are as follows [Eqs. (1) and (2)]:

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

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

with H_2P, HP^-, and P^{2-} being the free base, singly and doubly deprotonated forms of **I** and **II**.

We calculated total acidity constants of the both processes with Eq. (3). The calculated total acidity constants ($k_a = k_1 \times k_2$) were of: $k_a = 4.47 \cdot 10^{-13}$ (pk_a = 12.34) (**I**) and $k_a = 9.33 \cdot 10^{-14}$ (pk_a = 13.03) (**II**) (in acetonitrile, at 298 K).

$$\log k_a = \log Ind + n \log c_{DBU},\ n = 2, \quad (3)$$

where k_a, total acidity constant; *Ind*, the indicator ratio, $[P^{2-}]/[H_2P]$; c_{DBU}, the measured concentration of DBU,

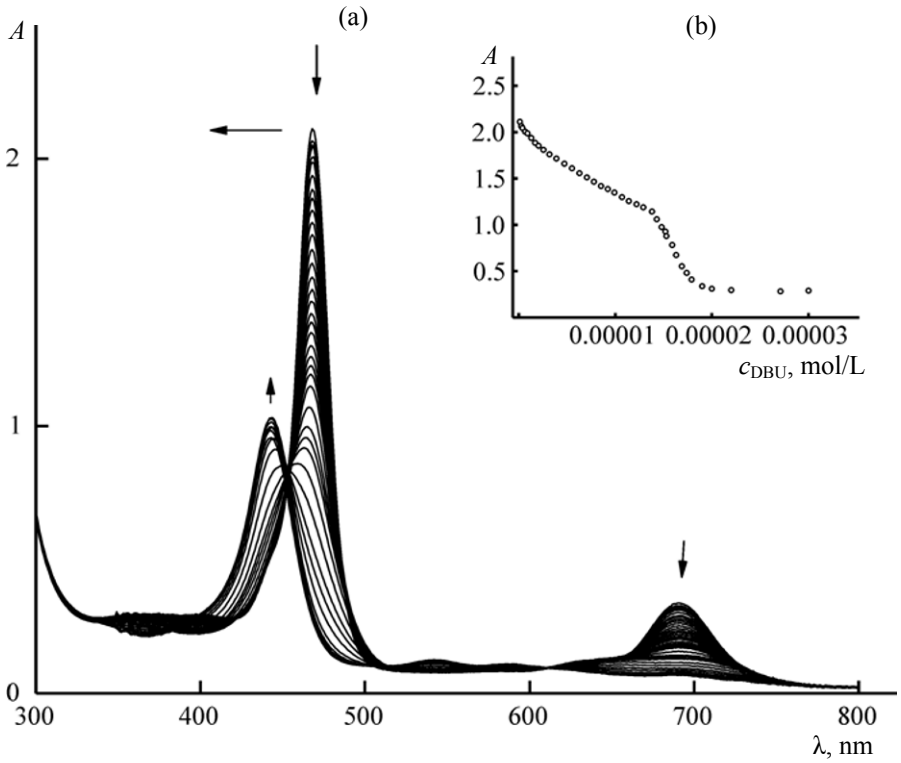


Fig. 1. (a) Electron absorption spectra of **I** ($c_{\mathbf{I}} = 2.30 \times 10^{-5}$ mol/L, c_{DBU} = 0–3×10^{-5} mol/L) and (b) the titration curve of **I** ($c_{\mathbf{I}} = 2.30 \times 10^{-5}$ mol/L) with DBU solution in acetonitrile, λ 468 nm, 298 K.

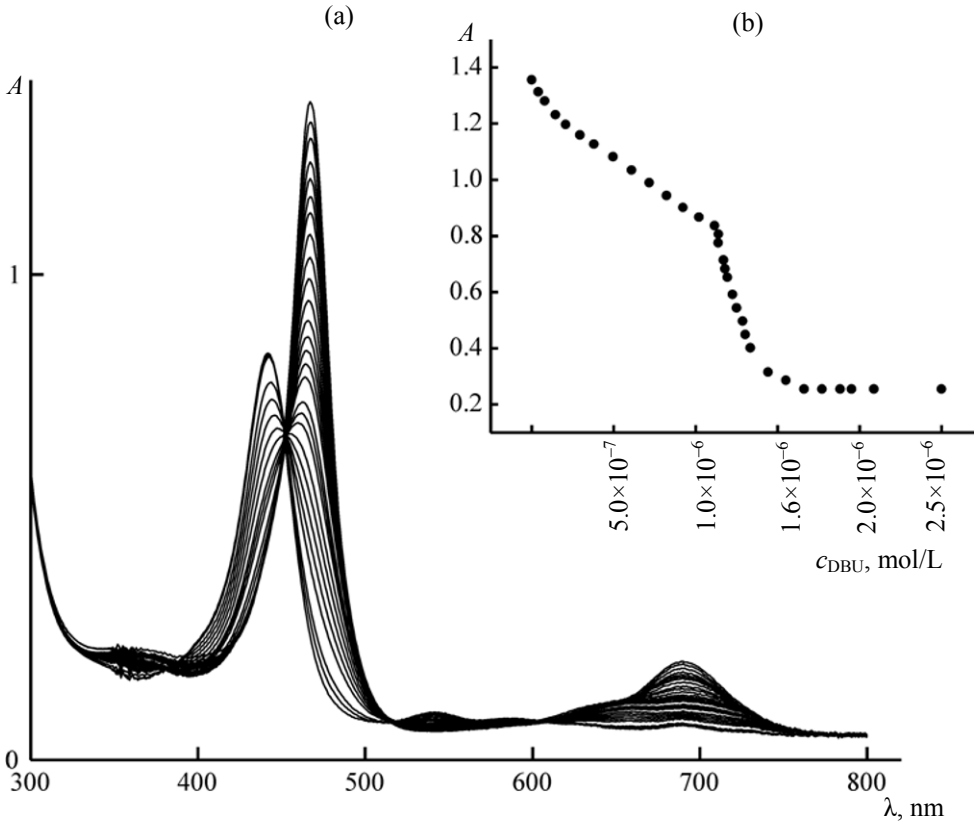


Fig. 2. (a) Electron absorption spectra of **II** ($c_{\mathbf{II}} = 1.8\times10^{-6}$ mol/L, $c_{DBU} = 0–2.5\times10^{-6}$ mol/L) and (b) the titration curve of **II** ($c_{\mathbf{II}} = 1.8\times10^{-6}$ mol/L) with DBU solution in acetonitrile, λ 467 nm, 298 K.

mol/L; $n = 2$, the number of protons bound to titrant per porphyrin molecule.

Accounting for the reactions (1) and (2) and the material balance [Eq. (4)], we obtained the fractions of the molecular and deprotonated forms of **I** and **II** in the course of titration.

$$c_0 = c(H_2P) + c(HP^-) + c(P^{2-}). \quad (4)$$

From Fig. 3, at DBU concentration of 2.7×10^{-5} mol/L (in the case of **I**) and of 2.09×10^{-6} mol/L (in the case of **II**) practically all the porphyrin molecules existed in the doubly deprotonated form. The calculation details are described in [10].

Analysis of the literature [11–15] showed that the introduction of bulky substituents in the *meso*- and β-pyrrole positions of the porphyrin macrocycle caused significant changes in the geometry of the molecules affecting their physical and chemical properties, including the bands positions in the electron absorption spectra. The spectral data from this work (see table) suggested the strongly deformed macrocycles structure in **I** and **II** as compared with their planar analogs, 2,3,7,8,12,13,17,18-octamethylporphyrin and 5,10,15,20-tetraphenylporphyrin (the bathochromic shift of the first absorption band was of $\Delta\lambda \approx 70–50$ nm and that of the Soret band was of $\Delta\lambda \approx 65–40$ nm). Spatial

Parameters of electronic absorption spectra of the free bases and products of their titration with DBU in acetonitrile

Porphyrin	Soret λ (log ε)	Soret λ_1 (log ε)
H_2OMP	400 (5.61)	620 (3.65)
H_2TPP	419 (5.69)	648 (3.80)
I	468 (5.96)	691 (5.16)
P^{-1} (**I**)	465 (5.59)	693 (5.79)
P^{2-} (**I**)	444 (5.61)	544 (4.73)
II	467 (5.87)	691 (5.04)
P^- (**II**)	465(5.66)	689 (4.84)
P^{2-} (**II**)	442 (5.65)	541 (4.52)

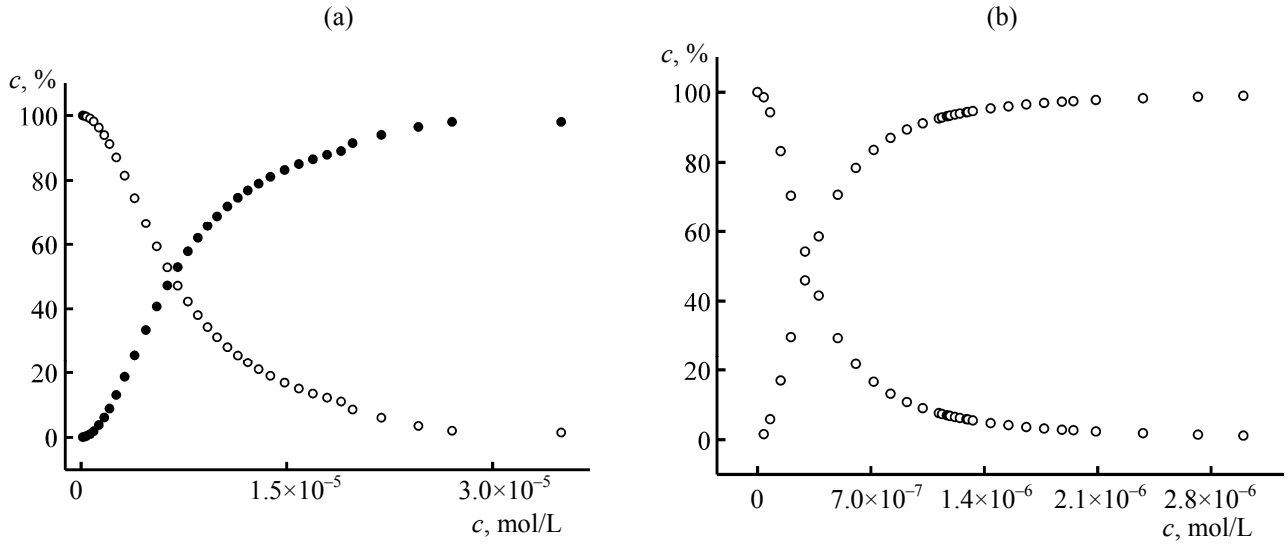


Fig. 3. Fractions of the doubly deprotonated and the molecular forms in the course of titration: (a) **I** and (b) **II**.

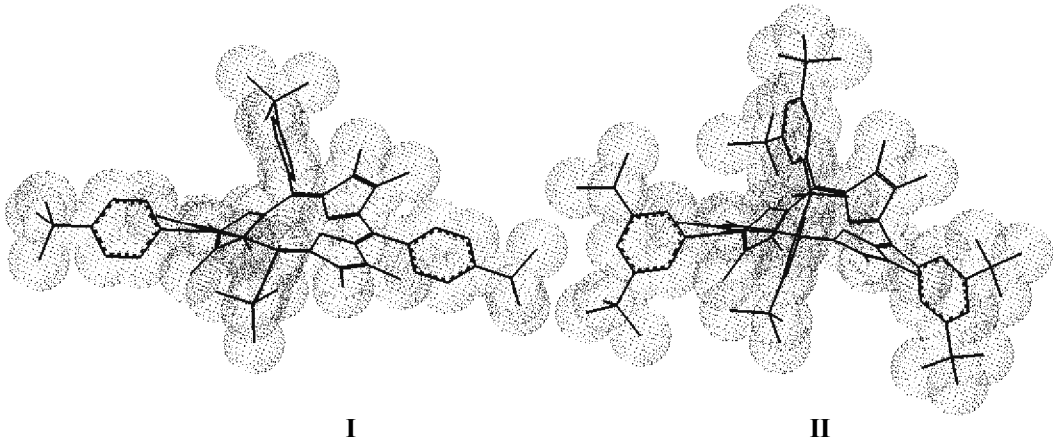


Fig. 4. Spatial structure of porphyrins **I** and **II** as simulated by the PM3 method.

structures of **I** and **II** as simulated by the semi-empirical quantum chemical PM3 calculations (HyperChem software) are shown in Fig. 4. In **I** and **II**, the phenyl fragments were rotated by 75°–90° with respect to the macrocycle plane, and hence could only affect the N_4 reaction site through the σ-bonds (*–I*-effect). Therefore, the introduction of the four phenyl substituents in the porphyrin macrocycle reduced the negative charge at the central nitrogen atoms, facilitating the N–H bonds cleavage. Methyl groups in the pyrrole β-positions induced the opposite effect (*+I*). However, those factors seemingly had no significant effect on the acidic properties of porphyrins **I** and **II**, the deformation of the macrocycle structure playing the decisive part. Introduction of the second *tert*-butyl group in the benzene fragment of *meso*-substituent of porphyrin **II** led to further distortion of the planar structure, being consistent with the acidity increase of **II** by almost 20 times.

EXPERIMENTAL

Preparation of 5,10,15,20-tetrakis(4'-*tert*-butylphenyl)-2,3,7,8,12,13,17,18-octamethylporphin (I) (*M* = 951.39). 2 mL of concentrated hydrobromic acid was added to solution of 1.0 g (10.5 mmol) of 3,4-dimethylpyrrole and 1.8 mL (10.8 mmol) of 4-*tert*-butylbenzaldehyde in 50 mL of methanol under carbon dioxide upon stirring. The mixture was stirred at room temperature during 1 h, diluted with 90 mL of THF, and 1.84 g (7.88 mmol) of 2,3,5,6-tetrachloro-*p*-benzoquinone was added upon stirring. The mixture was stirred at room temperature during 4 h (after 3 h, 1 mL of diethylamine was added). The solvent was removed, and the residue was mixed with alkali

solution upon heating, filtered off, washed with water, and dried in air at 70°C. The residue was dissolved in methylene chloride and purified by chromatography on alumina (Brockmann II grade), eluting with methylene chloride. The solvent was distilled off, and porphyrin was precipitated with methanol. Yield 0.49 g. The filtrate was evaporated to dryness, dissolved in methylene chloride, and purified by chromatography again. The solvent was evaporated to the minimum volume, the residue was diluted with methanol, and porphyrin was precipitated by adding small amount of water. The precipitate was filtered off and washed with methanol–water mixture (3:1). Yield 1.02 g (total yield 1.5 g, 60%). R_f (silufol) 0.67 (benzene-methanol, 3 : 1).

Synthesis of 5,10,15,20-tetrakis(3'5'-di-*tert*-butylphenyl)-2,3,7,8,12,13,17,18-octamethylporphin (II) (M = 1175.82). 2 mL of concentrated hydrobromic acid was added to solution of 1.0 g (10.5 mmol) of 3,4-dimethylpyrrole and 2.3 g (10.5 mmol) of 3,5-di-*tert*-butylbenzaldehyde in 50 mL of methanol under carbon dioxide upon stirring. The mixture was stirred at room temperature during 1 h, the porphyrinogen precipitate was filtered off and dried in air at room temperature. Yield 2.4 g (2.03 mmol). The resulting porphyrinogen was dissolved in 30 mL of THF, and suspension of 1.5 g (6.1 mmol) of 2,3,5,6-tetrachloro-*p*-benzo-quinone in 30 mL of THF was added. The solution was stirred at room temperature during 4 h, the solvent was distilled off; the residue was stirred with solution of potassium hydroxide, filtered off, washed with water and dried in air at 70°C. The product was dissolved in methylene chloride and purified by chromatography on alumina (Brockmann II grade), eluting with methylene chloride. The eluate was evaporated, and the product was precipitated by adding aqueous methanol. Yield 0.47 g (15.2%), R_f (silufol) 0.66 (benzene–methanol, 3 : 1).

Spectrophotometric titration with DBU in acetonitrile was performed using Varian Cary 100 spectrophotometer. The experimental procedure and the processing of the experimental data were similar to the procedures described in [8, 9]. Error of the dissociation constants determination was typically of 3–5%.

The initial porphyrins existed in the neutral molecular form when dissolved in dipolar aprotic acetonitrile (extra pure grade, water content of below 0.03%). Acetonitrile was further purified using the standard method [16]. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) was used as deprotonating agent, the ionization constant of its conjugate acid in acetonitrile being of pK_a = 13.2 [17]. An important advantage of the selected organic base over alkali was its excellent solubility in organic solvents.

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