ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 5, pp. 991–996. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © O.V. Toldina, N.Zh. Mamardashvili, 2008, published in Zhurnal Obshchei Khimii, 2008, Vol. 78, No. 5, pp. 848–853.

Synthesis of 2,8,12,18-Tetrabutyl-3,7,13,17-tetramethyl-5-{3-[11-(pyridin-4-yloxy)-3,6,9-trioxaundecyloxy]phenyl}-porphyrin and Study on the Effect of Its Molecular Conformation on Physicochemical Properties

O. V. Toldina and N. Zh. Mamardashvili

Institute of Solution Chemistry, Russian Academy of Sciences,
ul. Akademicheskaya 1, Ivanovo, 153045 Russia
e-mail: Olga_Toldina@mail.ru

Received July 13, 2007

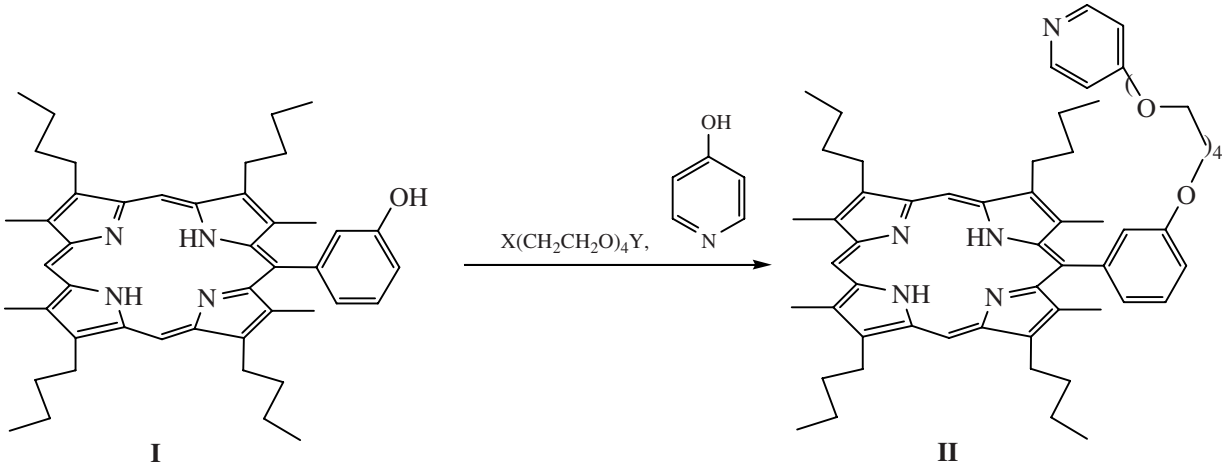
Abstract—2,8,12,18-Tetrabutyl-3,7,13,17-tetramethyl-5-{3-[11-(pyridin-4-yloxy)-3,6,9-trioxaundecyloxy] phenyl}porphyrin was synthesized, and its complexation with zinc and potassium cations in the system toluene–methanol (5:1) was studied by spectrophotometric titration and ^{1}H NMR spectroscopy. Spatial preorganization of the *meso*-aryl substituent due to complex formation of potassium cation with the polyether fragment accelerates the reaction of zinc with the title compound approximately threefold. A probable scheme of the interaction was proposed, and formation constants of the corresponding complexes were determined.

DOI: 10.1134/S1070363208050265

Porphyrins occupy a quite specific place [1–5] among numerous macroheterocyclic compounds capable of forming self-organized supramolecular ensembles and functional devices based thereon via multicenter interactions. Importance of studies in this field is determined by selectivity and high sensitivity of tetrapyrrole macrorings to low-energy impacts which make it possible to establish control over chemical processes with participation of such structures. Chemically modified porphyrins attract specific interest, for the reactivity of the coordination entity therein can be essentially varied (controlled) via introduction of appropriate peripheral substituents into the *meso* positions or β-positions of the pyrrole rings [6]. Supramolecular systems based on modified porphyrins could give rise to molecular devices capable of reversibly changing their steric structure, properties, and functionality by the action of external factors, e.g., light pulse duration, acid–base interactions, and complex formation with various substrates. Although the available published data demonstrate importance and wide prospects in practical application of tetrapyrrole macrorings [7, 8], no detailed interpretation of the effects of electronic and structural factors on the selectivity of tetrapyrroles has been given up to now.

In the recent years, interest in the chemistry of porphyrins has increased sharply due to ability of these compounds to act as receptors in molecular recognition, i.e., highly selective intermolecular interaction only with a definite type of molecules [3, 4, 9]. From this viewpoint, specifically interesting are porphyrin molecules containing peripheral crown ether or polyethylene oxide fragments which possess proper complexing ability toward various substrates [6]. With a view to obtain spatially preorganized three-dimensional systems possessing qualitatively different functionalities as compared to particular molecular components, we have synthesized a supramolecule consisting of covalently bonded porphyrin, tetraethylene oxide, and pyridine fragments. The reaction of *meso*-(3-hydroxyphenyl)porphyrin **I**, tetraethylene glycol bis(4-toluenesulfonate), and 4-hydroxypyridine in the presence of cesium carbonate in dimethylformamide–acetonitrile gave porphyrin **II** in which one of the *meso* positions in the macroring was occupied by conformationally labile polyether fragment having a terminal pyridine ring (Scheme 1). The elemental composition and electronic absorption, ^{1}H NMR, and mass spectra of compound **II** were fully consistent with the assumed structure.

Scheme 1.



I **II**

$X = CH_3C_6H_4SO_3$, $Y = CH_3C_6H_4SO_2$.

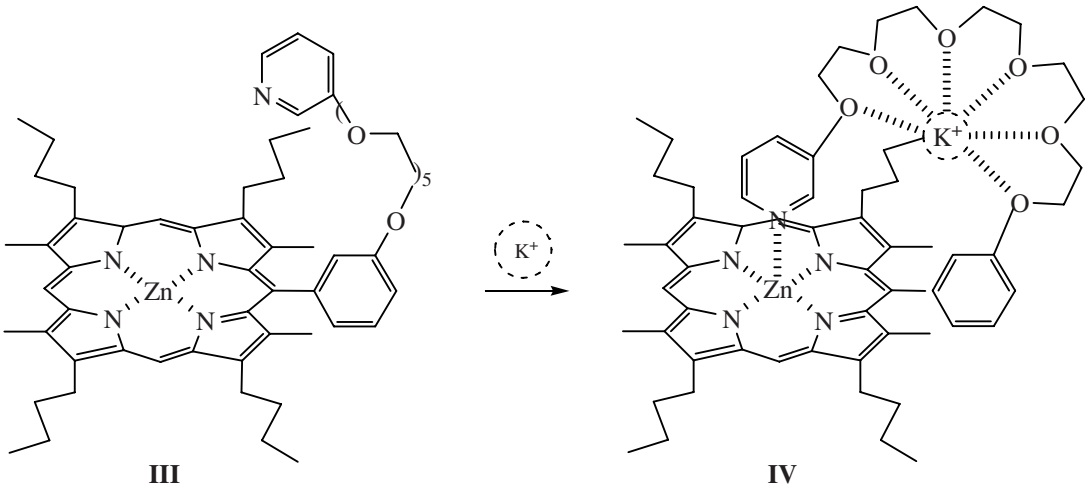
We previously found [10] that (2,8,12,18-tetrabutyl-3,7,13,17-tetramethyl-5-{3-[14-(pyridin-4-yloxy)-3,6,9,12-tetraoxatetradecyloxy]phenyl}porphyrinato) zinc(II) (**III**) is capable of binding potassium cations to give complex **IV** due to conformity of the geometric parameters of the pentaethylene oxide complexing cavity to the substrate dimensions (Scheme 2).

The complexation is accompanied by a change of the molecular conformation so that the pyridine fragment approaches the tetrapyrrole macroring. This is clearly observed in the electronic absorption and ^{1}H NMR spectra. Donor–acceptor interaction between the pyridine nitrogen atom and zinc cation induces a red shift of absorption bands (up to 10 nm) of the system Zn-porphyrin–potassium tetrafluoroborate, while shielding of the pyridine fragment by the porphyrin ring current leads to upfield shift of signals from protons in the pyridine ring (especially in the α-positions).

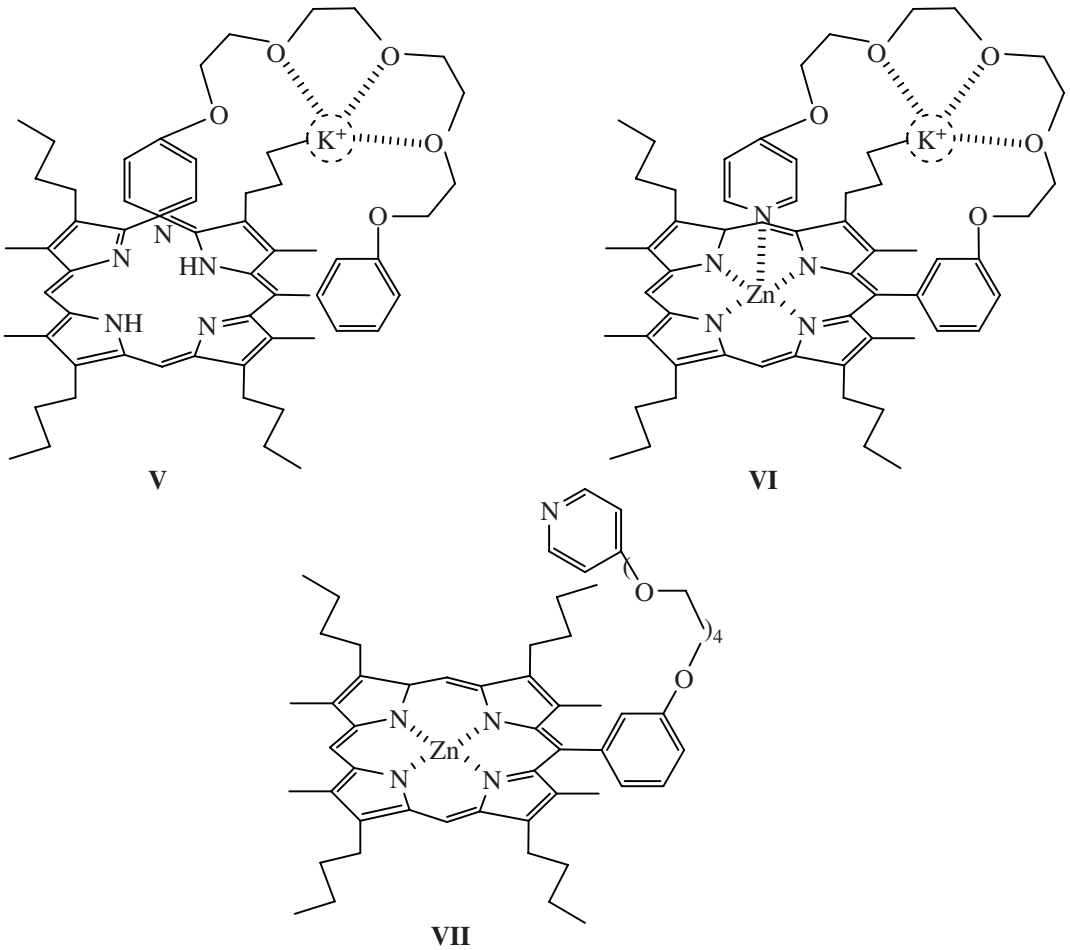
Spectrophotometric study on the complexation of compound **III** with potassium cations showed that complex **IV** has a composition of 1:1, and its stability constant K_s was estimated at 0.361×10^6 l mol^{-1} [10].

In the present work we found by ^{1}H NMR spectroscopy that complex formation of potassium cation with the tetraethylene oxide fragment of porphyrin **II**, as in supramolecular complex **IV**, is

Scheme 2.



III **IV**



accompanied by conformational reorganization leading to approach of the pyridine fragment to the tetrapyrrole macroring. In the ^{1}H NMR spectrum of complex **V**, signals from protons in the pyridine ring are displaced upfield ($\Delta\delta$ = 4.0 ppm relative to pure pyridine) due to the shielding by the porphyrin ring current.

The reaction of zinc cation with porphyrin **II** in toluene–methanol (5:1) is characterized by a rate constant k_v^{298} of 3.055×10^{-2} l mol^{-1} s^{-1} ($c_{\mathbf{II}} = 1\times10^{-5}$ M, $c_{Zn} = 1\times10^{-3}$ M). Under analogous conditions, but in the presence of potassium cations (complex **V**) the reaction with zinc(II) acetate to give complex **VI** is faster by a factor of 3 ($k_v^{298} = 9.687\times10^{-2}$ l mol^{-1} s^{-1}).

In keeping with published data, apart from such factors as solvent and metal ion natures, the rate of formation of porphyrin–metal complex strongly depends on structural specificity of the porphyrin molecule. At the activation stage, tetrapyrrole macroring undergoes considerable transformations. In particular, it loses two central hydrogen atoms as protons which are then solvated by the solvent [10]. Therefore, the rate of formation of porphyrin–metal complex and activation parameters of the process depend on the electron density on the nitrogen atoms in the coordination entity, which is determined in turn by substituent effects and molecular conformation.

Presumably, complexation of potassium cation by the polyether fragment forces the *meso*-substituent to arrange in such a way that the zinc ion interacts simultaneously with lone electron pairs on two nitrogen atoms in the coordination entity of the tetrapyrrole macroring and nitrogen atom in the pyridine ring (Fig. 1). Zinc(II) cation tends to adopt sp^3 or d^2sp^2 hybridization, but in the planar porphyrin molecule it ought to gain dsp^2 configuration with electron-deficient $4p_z$ and $4d_{z^2}$ orbitals that are involved in donor–acceptor interaction with the electron-donor pyridine nitrogen atom. Study on the complex formation of zinc cation with porphyrin **I** in the presence and in the absence of potassium cations

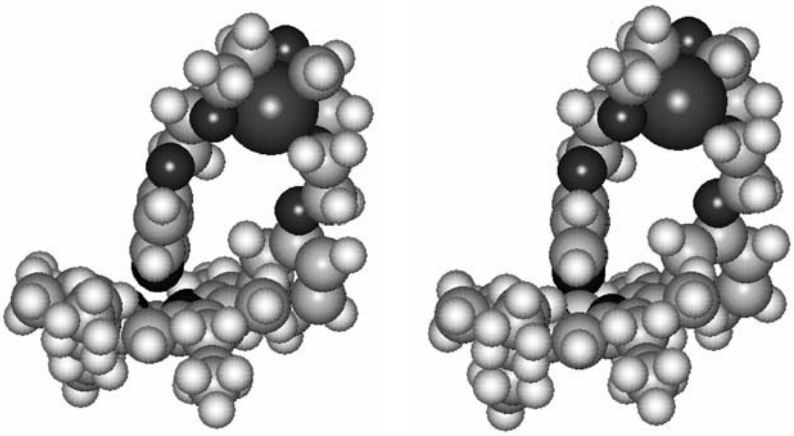


Fig. 1. Structures of compounds **V** and **VI** optimized by the MM+ method using HyperChem program.

showed that the potassium almost does not affect the coordination process [11]. According to the ^{1}H NMR data, in the absence of potassium cation the pyridine fragment is fairly distant from the coordination entity (protons in the pyridine ring do not suffer from shielding effect of the porphyrin ring current), and the pyridine nitrogen atom is not involved in coordination.

Probably, the entropy factor related to fixation of the pyridine fragment over the coordination entity of the tetrapyrrole macroring in complex **III** favors binding of zinc cation. Our results indicate exceptional importance of steric configuration and mutual spatial arrangement of components in supramolecular systems, and they can be used in the design of functional nanosize materials for the determination and separation of various biologically active substrates.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker VC-200 spectrometer at a frequency of 200 MHz using chloroform-*d* as solvent and tetramethylsilane as internal reference. The electron-impact mass spectra (70 eV) were obtained on an MKh-1310 instrument (ion source temperature 150–200°C).

2,8,12,18-Tetrabutyl-5-(3-hydroxyphenyl)-3,7,13,17-tetramethylporphyrin (**I**) was synthesized according to the procedure described in [12]. Tetraethylene glycol bis(4-toluenesulfonate) and 4-hydroxypyridine were commercial reagents (Acros). Individual compounds were isolated by column chromatography on neutral aluminum oxide using methylene chloride–hexane (1:1) as eluent. Organic solvents were purified by standard procedures [13]. The progress of reactions was monitored by TLC on Silufol UV-254 plates.

Procedure for kinetic experiments. Accurately measured volumes of preliminarily prepared solutions of porphyrin **II** ($c_{\mathbf{II}} = 1\times10^{-5}$ M) and zinc(II) acetate ($c_{Zn} = 1\times10^{-3}$ M) in a mixed solvent were placed in glass cells, adjusted to a required temperature (298–318 K), and thoroughly mixed. The complex formation progress was monitored by spectrophotometry using a Cary 100 spectrophotometer by measuring the optical density of the reaction mixture at λ = 511 nm at definite time intervals. The spectra clearly displayed isosbestic points both in the presence and in the absence of potassium ions (Fig. 2).

Coordination of porphyrins by metal acetates is described by the following equation:

$$H_2P + MAc_2 \rightarrow MP + 2HAc. \quad (1)$$

The process conforms to the following kinetic equation:

$$-dc_{\mathbf{II}}/dt = k_v c_{\mathbf{II}} c_{Zn}. \quad (2)$$

Here, k_v is the rate constant of reaction (1), and $c_{\mathbf{II}}$ and c_{Zn} are the concentrations of porphyrin **II** and zinc (II) acetate, respectively. The reaction is characterized by first order with respect to both porphyrin **II** and zinc salt. Kinetic experiments were performed using a 100-fold excess of zinc(II) acetate with respect to porphyrin **II**; the rate constant k_v was calculated using the following equation:

$$k_v = k_{ap}/c_{Zn} = \ln [(A_0 - A_\infty)/(A_\infty - A_\tau)]/(\tau\, c_{Zn}). \quad (3)$$

Here, A_0, A_∞, and A_τ are the optical densities of the reaction mixture at the initial moment, by the end of the reaction, and at a time τ, respectively. The error in the determination of k_{ap} was ±(3–5)%.

2,8,12,18-Tetrabutyl-3,7,13,17-tetramethyl-5-{3-[11-(pyridin-4-yloxy)-3,6,9-trioxaundecyloxy]phenyl}-

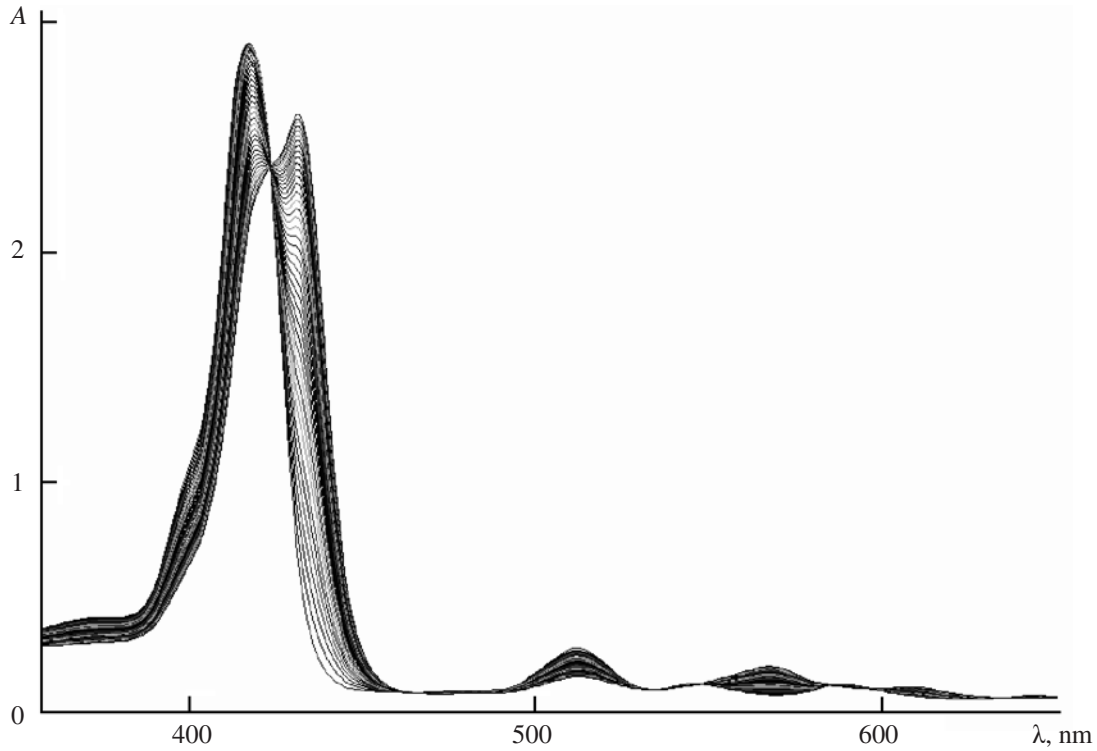


Fig. 2. Variation of the electronic absorption spectrum in the complex formation of porphyrin **II** with zinc(II) acetate.

porphyrin (II). Porphyrin **I**, 100 mg, and 4-hydroxypyridine, 12.84 mg, were dissolved in 9 ml of a 1:2 mixture of dimethylformamide and acetonitrile, and 32.51 mg of cesium carbonate and 42.96 mg of tetraethylene glycol bis(4-toluenesulfonate) were added under nitrogen. The mixture was stirred for 24 h at 100°C, the solvent was distilled off under reduced pressure, and the residue was treated with 30 ml of methylene chloride containing 5 ml of 10% hydrochloric acid. The organic layer was separated, washed with two portions of water, dried over sodium sulfate, and evaporated to a volume of 20 ml, and the residue was subjected to chromatography on aluminum oxide using methylene chloride–hexane (1:1) as eluent. The solvent was distilled off from the eluate under reduced pressure, and the residue was recrystallized from methylene chloride–methanol (1:1). Yield 36.16 mg (32%), R_f 0.49 (Al_2O_3, CH_2Cl_2–C_6H_{14}, 1:2). Electronic absorption spectrum (toluene), λ_{max}, nm (log ε): 406.2 (4.89), 507.5 (4.04), 542.1 (3.49), 573.8 (3.71), 627.13 (3.16). ^{1}H NMR spectrum, δ, ppm: 10.03 s (2H, *meso*-H), 9.96 s (1H, *meso*-H), 7.91 d (1H, *o*-H), 7.83 s (1H, *o*-H), 7.65 d (2H, 3′-H), 7.56 t (1H, *m*-H), 7.49 d (2H, 2′-H), 7.29 d (1H, *p*-H), 3.80 m (8H, CH_2CH_2·CH_2CH_3), 3.26 m (16H, OCH_2CH_2O), 2.40 q (8H, $CH_2CH_2CH_2CH_3$), 1.50 m (8H, $CH_2CH_2CH_2CH_3$), 1.20 s (6H, CH_3), 1.14 s (6H, CH_3), 1.01 t (12H, $CH_2CH_2CH_2CH_3$), –2.62 s (2H, NH). Mass spectrum, *m/z* (I_{rel}, %): 933.98 (72) $[M]^+$. Found, %: C 75.68; H 8.20; N 7.44. $C_{59}H_{77}N_5O_5$. Calculated, %: C 75.72; H 8.23; N 7.48.

^{1}H NMR spectrum of complex **V**, δ, ppm: 10.04 s (2H, *meso*-H), 9.96 s (1H, *meso*-H), 7.90 d (1H, *o*-H), 7.81 s (1H, *o*-H), 7.56 t (1H, *m*-H), 7.27 d (1H, *p*-H), 6.37 d (2H, 3′-H), 3.78 m (8H, $CH_2CH_2CH_2CH_3$), 3.48 d (2H, 2′-H), 3.23 m (16H, OCH_2CH_2O), 2.38 q (8H, $CH_2CH_2CH_2CH_3$), 1.48 m (8H, $CH_2CH_2CH_2CH_3$), 1.19 s (6H, CH_3), 1.12 s (6H, CH_3), 1.00 t (12H, $CH_2CH_2CH_2CH_3$), –2.58 s (2H, NH).

^{1}H NMR spectrum of (2,8,12,18-tetrabutyl-3,7,13,17-tetramethyl-5-{3-[11-(pyridin-4-yloxy)-3,6,9-trioxaundecyloxy]phenyl}porphyrinato)zinc(II) (**VII**), δ, ppm: 10.00 s (2H, *meso*-H), 9.92 s (1H, *meso*-H), 7.89 d (1H, *o*-H), 7.81 s (1H, *o*-H), 7.63 d (2H, 3′-H), 7.51 t (1H, *m*-H), 7.45 d (2H, 2′-H), 7.27 d (1H, *p*-H), 3.78 m (8H, $CH_2CH_2CH_2CH_3$), 3.21 m (16H, OCH_2CH_2O), 2.39 q (8H, $CH_2CH_2CH_2CH_3$), 1.47 m (8H, $CH_2CH_2CH_2CH_3$), 1.18 s (6H, CH_3), 1.12 s (6H, CH_3), 1.03 t (12H, $CH_2CH_2CH_2CH_3$).

^{1}H NMR spectrum of complex **VI**, δ, ppm: 9.97 s (2H, *meso*-H), 9.89 s (1H, *meso*-H), 7.85 d (1H, *o*-H), 7.78 s (1H, *o*-H), 6.28 d (2H, 3′-H), 7.48 t (1H, *m*-H), 3.41 d (2H, 2′-H), 7.25 d (1H, *p*-H), 3.75 m (8H, $CH_2CH_2CH_2CH_3$), 3.19 m (16H, OCH_2CH_2O), 2.35 q (8H, $CH_2CH_2CH_2CH_3$), 1.45 m (8H, CH_2CH_2·CH_2CH_3), 1.17 s (6H, CH_3), 1.11 s (6H, CH_3), 1.01 t (12H, $CH_2CH_2CH_2CH_3$).

ACKNOWLEDGMENTS

This study was performed under financial support by the Russian Foundation for Basic Research (project nos. 06-03-81001-Bel, 05-03-32055) and by the Chemistry and Materials Science Division, Russian Academy of Sciences (program no. 7, "Chemistry and Physical Chemistry of Supramolecular Systems and Atom Clusters," state contract no. 02.513.11.3229).

REFERENCES

1. Ogoshi, H., Mizutani, T., Hayashi, T., and Ruroda, Y., *The Porphyrin Handbook*, Kadish, K.M., Smith, K.M., and Guilard, R., Eds., San Diego: Academic, 2000, vol. 6, p. 280.
2. Sanders, J.K.M., *The Porphyrin Handbook*, Kadish, K.M., Smith, K.M., and Guilard, R., Eds., San Diego: Academic, 2000, vol. 3, p. 347.
3. Wojaczyński, J. and Latos-Grażński, L., *Coord. Chem. Rev*., 2000, vol. 204, no. 1, p. 133.
4. Fleischer, E.B. and Shachter, A.M., *Inorg. Chem*., 1991, vol. 30, no. 19, p. 3763.
5. Gardner, M., Guerin, A.J., Hunter, C.A., Michelsen, U., and Rotger, C., *New J. Chem*., 1999, no. 23, p. 309.
6. Koifman, O.I., Mamardashvili, N.Zh., and Antipin, I.S., *Sinteticheskie retseptory na osnove porfirinov i ikh kon"yugatov s kaliks[4]arenami* (Synthetic Receptors on the Basis of Porphyrins and Their Conjugates with Calix[4]arenes), Moscow: Nauka, 2006, p. 246.
7. Mamardashvili, G.M., Mamardashvili, N.Zh., and Koifman, O.I., *Usp. Khim*., 2005, vol. 74, no. 8, p. 839.
8. Berezin, B.D., *Koordinatsionnye soedineniya porfirinov i ftalotsianina* (Coordination Compounds of Porphyrin and Phthalocyanine), Moscow: Nauka, 1978, p. 279.
9. Mamardashvili, G.M., Kumeev, R.S., and Mamardashvili, N.Zh., *Zh. Neorg. Khim*., 2006, vol. 51, no. 8, p. 1349.
10. Ivanova, Yu.B., Toldina, O.V., Sheinin, V.B., and Mamardashvili, N.Zh., *Russ. J. Org. Chem*., 2007, vol. 43, no. 9, p. 1397.
11. Toldina, O.V. and Mamardashvili, N.Zh., Abstracts of Papers, *IVth Int. Symp. "Design and Synthesis of Supramolecular Architectures,"* Kazan (Russia), 2006, p. 106.
12. Mamardashvili, N.Zh., Abstracts of Papers, *XXV nauchnaya sessiya Vserossiiskogo seminara po khimii porfirinov i ikh analogov* (XXVth Scientific Session of the All-Russian Seminar on the Chemistry of Porphyrins and Their Analogs), Ivanovo, 2004, p. 13.
13. *Organikum. Organisch-chemisches Grundpraktikum*, Berlin: Wissenschaften, 1976, 15th edn. Translated under the title *Organikum*, Moscow: Mir, 1979, vol. 2, p. 422.