

Synthesis and Properties of Zinc Complexes of *meso*-Hexadecyloxy-Substituted Tetrabenzoporphyrin and Tetrabenzoazaporphyrins

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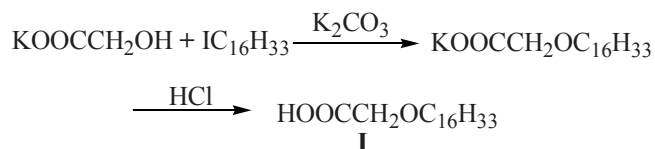
Abstract—The hexadecyloxyacetic acid was prepared by alkylation of glycolic acid. Proceeding from the acid obtained zinc complexes were synthesized of *meso-trans*-di(hexadecyloxy)tetra-benzoporphyrin, *meso-tetra*(hexadecyloxy)tetrabenzoporphyrin, and also of *meso*-hexadecyloxytetrabenzoazaporphyrins. The spectral properties of compounds synthesized were investigated.

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Zinc complexes of *meso*-aryl-substituted tetrabenzoporphyrins possess unique electronic optical properties and therefore attract now much attention of researchers as materials for diagnostics and treatment of malign tumors [1, 2], and also as limiting media for laser emission [3].

In this respect *meso*-alkoxy-substituted tetrabenzoporphyrins and their derivatives may also be of a considerable interest. However this kind porphyrins were not investigated up till now due to the lack of preparative procedures for their synthesis. Therefore the goal of this study was a development of preparation procedure and investigation of spectral properties of zinc complexes of *meso*-hexadecyloxy-substituted tetrabenzoporphyrins and their aza derivatives.

The hexadecyloxyacetic acid (**I**) necessary for the synthesis of these compounds was obtained by alkylating potassium glycolate with 1-hexadecyl iodide in DMF in the presence of potassium carbonate by boiling the mixture for 5 h.



On finishing the heating the unreacted 1-hexadecyl iodide was removed from the reaction mixture by steam distillation, then the mixture was cooled and acidified

with hydrochloric acid to pH 2. The precipitated acid **I** was filtered off, washed with water, and dried.

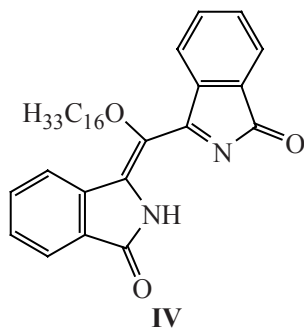
Acid **I** is a waxy light-yellow substance soluble in alkaline water solutions and in organic solvents. Its structure was confirmed by elemental analysis, vibration and ¹H NMR spectra.

IR spectrum of compound **I** contained strong bands in the region 2954, 2917, 2849, and 1467 cm⁻¹ characteristic of the stretching vibrations of the C–H bonds, a band at 1731 cm⁻¹ indicating the presence of a carboxy group, and bands at 1179 and 1058 cm⁻¹ corresponding to the stretching vibrations of C–O bonds of the ether group.

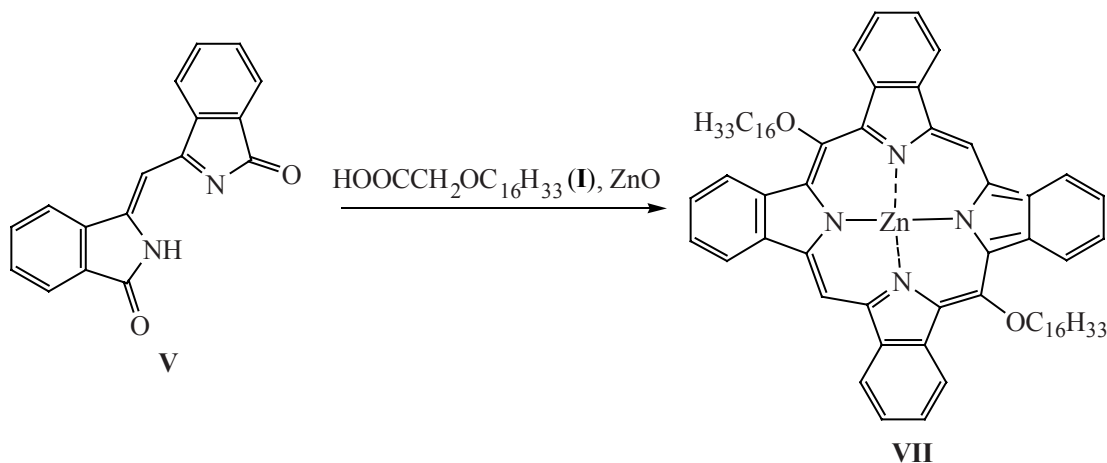
In the ¹H NMR spectrum of compound **I** the most downfield singlet signal belonged to the proton of the carboxy group at 10.55 ppm, the doublet at 4.05–3.92 ppm corresponded to the resonance of two protons of the methylene group contiguous to the carboxyl, the triplet at 3.65 ppm was characteristic of two protons of the α-methylene group of the alkyl substituent, the singlet at 2.16 ppm was due to two protons of the β-methylene group, the singlet at 1.24 ppm originated from the resonance of 26 protons of the other methylene groups, and finally, the singlet at 0.85 ppm belonged to three protons of the terminal methyl group.

We attempted to synthesize zinc *meso*-tetra(hexadecyloxy)tetrabenzoporphyrinate (**II**) by heating acid **I** with phthalimide (**III**) in the presence of zinc oxide at various

reagents ratios. However all attempts failed. The cause of the failure was the low thermal stability of compound **I**. The presence of an alkoxy group in the molecule of acid **I** resulted in a relatively low temperature of the start of decarboxylation (220–250°C), therefore the reaction of compound **I** with imide **III** ended apparently on the stage of formation of 3-[1-(3-oxo-2,3-dihydro-1*H*-isoindol-1-yl)-1-hexadecyloxymethylidene]-1-isoindolinone (**IV**). This assumption is in agreement with the dark-red color of the reaction mixture, and also with the presence in its mass spectrum of a peak of m/z 514 corresponding to a molecular ion of compound (**IV**). The raising of the temperature to 350°C did not lead to the formation of zinc complex **II** in measurable quantities. Presumably under these conditions the thermal decomposition both of acid **I** and its condensation products with phthalimide (**III**) prevailed over the process of the formation of porphyrin macrocycle.



This situation required to use in the synthesis of the target metal complexes more active reagents than phthalimide (**III**). Such compounds are 3-[1-(3-oxo-2,3-dihydro-1*H*-isoindol-1-yl)methylidene]-1-isoindolinone (**V**) obtained by procedure [4] by condensation of imide **III** with zinc acetate, and also 1,3-diiminoisoindoline (**VI**).

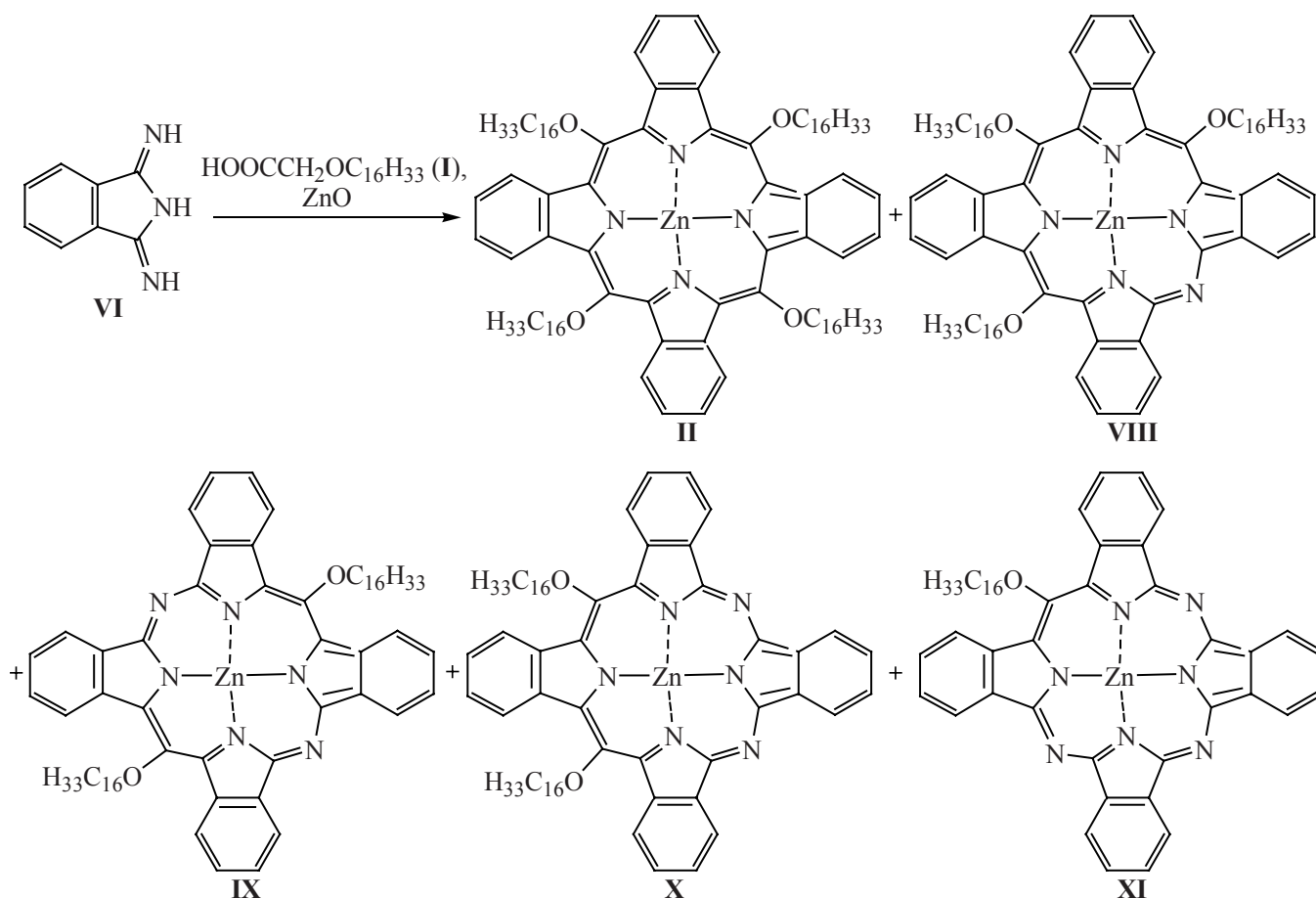


The reaction of compound **V** with acid **I** in the presence of zinc oxide at 300°C within 30 min resulted in the formation of zinc *meso-trans*-di(hexadecyloxy)tetraenzoporphyrinate (**VII**).

Complex **VII** was isolated from the reaction mixture by column chromatography. It is a dark-green powder well soluble in polar and nonpolar organic solvents. The structure of compound **VII** was confirmed by elemental analysis, electronic and ^1H NMR spectroscopy.

In the ^1H NMR spectrum of compound **VII** appears a multiplet in the region 7.80–7.30 ppm corresponding to the resonance of 16 protons of the benzene rings of the isoindole fragments, a triplet at 4.01 ppm is characteristic of the resonance of four protons of two α -methylene groups of the alkoxy substituents, a multiplet in the region 2.17–2.11 ppm originates from the resonance of four protons of two β -methylene groups, a singlet at 1.19 ppm, from the resonance of 52 protons of the other methylene groups, and a singlet at 0.87 ppm belongs to the six protons of two terminal methyl groups. The resonance of two protons in the *meso*-positions of the macroring is observed as a singlet at 9.13 ppm.

The reaction of 1,3-diiminoisoindoline (**VI**) with aliphatic carboxylic acids in the presence of zinc oxide is known to give a mixture of *meso*-alkyl-substituted zinc tetraenzoporphyrinates, and the ratio of compounds with various content of aza groups depends on the molar ratio of the reagents [5]. We performed a reaction of compound **VI** with excess acid **I** in the presence of zinc oxide at 270°C for 45 min. The process provided a mixture of zinc complexes of *meso*-tetra(hexadecyloxy)tetraenzoporphyrin (**II**), *meso*-tri(hexadecyloxy)tetraenzomonoazaporphyrin (**VIII**), *meso-trans*-di(hexadecyloxy)tetraenzodiazaporphyrin (**IX**), *meso-cis*-di(hexadecyloxy)tetraenzodiazaporphyrin (**X**),



and *meso*-mono(hexadecyloxy)tetrabenzotriazaporphyrin (**XI**).

Complexes **II**, **VIII–XI** were isolated from the reaction mixture by column chromatography. They are wax-like (**II**, **VIII**) and powdery (**IX–XI**) green or blue-green substances well soluble in various organic solvents. Their structure was confirmed by elemental analysis, electronic and ^1H NMR spectroscopy.

The ^1H NMR spectrum of complex **II** is similar in pattern to the spectrum of compound **VII** and differs from the latter by the larger intensity of the proton signals from the aliphatic substituents, and by the absent resonances of protons in the *meso*-positions of the macroring. As to the ^1H NMR spectra of azaporphyrins **VIII–XI**, they also lack the signals of *meso*-protons, and the signals of the protons from the benzene rings of the isoindole fragments and from the alkoxy substituents are situated in the same regions as in the spectra of complexes **II** and **VII**.

The electron absorption spectrum of compound **VII** is characterized by the presence of a Q band with a maximum at 624 nm and a Soret band with a maximum at 424 nm. The

maxima of the absorption bands are in the same regions as in the spectrum of zinc tetrabenzoporphyrinate [6] suggesting a conclusion that the *meso*-alkoxy substituents insignificantly affect the electronic and geometrical structure of the tetrabenzoporphyrin macroring. A similar spectral pattern was previously mentioned for the *meso*-phenoxy-substituted zinc tetrabenzoporphyrinate [7]. Introducing into the molecule of porphyrin **VII** two more *meso*-alkoxy substituents as expected did not significantly affect the electron absorption spectrum. The maxima of Q band and Soret band in the spectrum of complex **II** (Fig. 1, 1) are located at 623 and 422 nm respectively.

Much more significant spectral changes are observed at introducing a nitrogen atom into the *meso*-position of the tetrabenzoporphyrin macroring. The electron absorption spectrum of complex **VIII** (Fig. 1, 2) although resembles the spectrum of compound **II** by the position of the main absorption bands, but is quite different from the latter by their intensity ratio. Whereas in the spectrum of complex **II** the intensity ratio of Q and Soret bands is 1:2.66, in going to compound **VIII** it alters to 1:1.62.

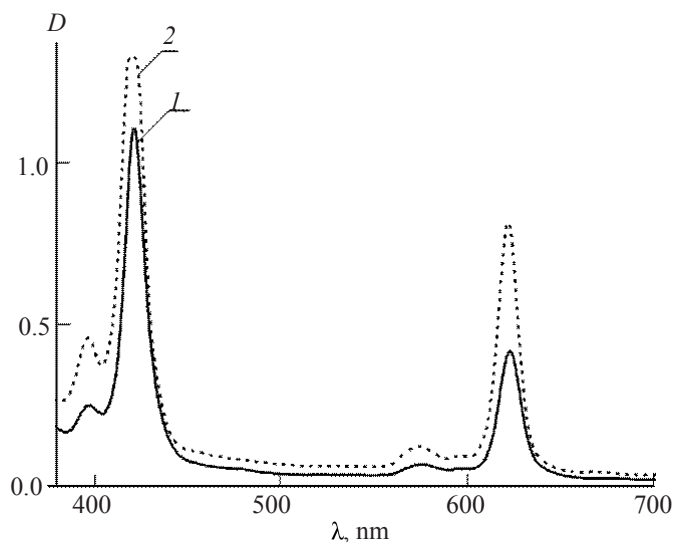


Fig. 1. Electron absorption spectra in chloroform solution. 1, zinc *meso*-tetra(hexadecyloxy)tetrabenzoporphyrinate (**II**), 2, zinc *meso*-tri(hexadecyloxy)tetrabenzomonoazaporphyrinate (**VIII**).

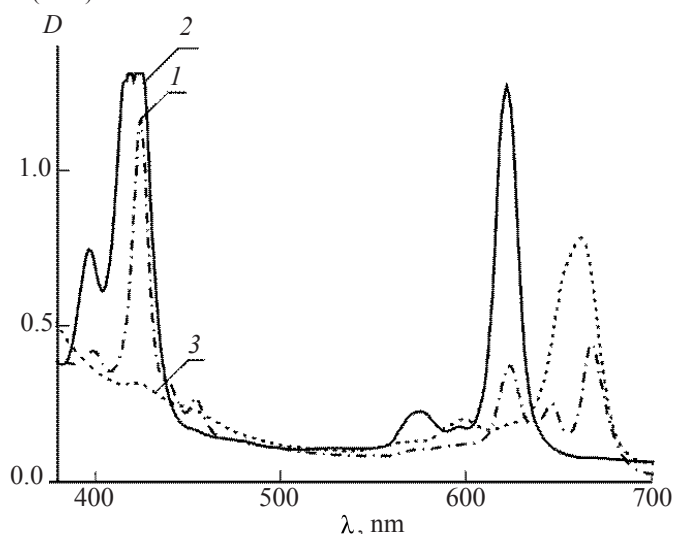


Fig. 2. Electron absorption spectra in chloroform solution. 1, zinc *meso*-*trans*-di(hexadecyloxy)tetrabenzodiazaporphyrinate (**IX**), 2, zinc *meso*-*cis*-di(hexadecyloxy)tetrabenzodiazaporphyrinate (**X**), 3, zinc *meso*-mono(hexadecyloxy)tetrabenzotriazaporphyrinate (**XI**).

The increase in the relative intensity of the Q band in the electronic spectrum of azaporphyrin **VIII** is likely due to the mutual approach of HOMO (A_{1g}) and LUMO (E_u) because of greater rigidity and aromaticity of the macroring.

Even greater changes in the spectral pattern are observed in going to diazaporphyryns **IX** and **X**. The electronic spectrum of *meso*-*trans*-substituted complex **IX** (Fig. 2, 1) in the region of the Q band is split in three bands. This fact may be caused by decreased symmetry

of the macroring and consequently the quasiforbidden electronic transitions from the orbital A_{1g} to two normally oriented orbitals E_u^* , degenerate in the case of porphyrins of D_{4h} symmetry (for instance, in their metal complexes) become permitted. In the porphyrazines of unsymmetrical structure the degeneration is released, and the Q band splits in two components of similar intensity [8] (band with the maxima at 668 and 623 nm). The bands with a maximum at 646 nm is likely to originate from the charge transfer from the donor part of the complex **IX** molecule to the acceptor part. A similar spectral pattern was also observed in phthalocyanines of unsymmetrical structure [9]. The Soret band in the spectrum of complex **IX** has a maximum at 425 nm, i.e., suffers a red shift by 5 nm as compared to the spectrum of compound **VIII** due to a somewhat greater polarization of the molecule **IX**. It should be also noted that in the spectrum of compound **IX** appears also a band with a maximum at 454 nm that also is a charge-transfer band.

In the electronic spectrum of *meso*-*cis*-substituted diazaporphyryn **X** (Fig. 2, 2) the degree of splitting of the Q band is smaller, and its relative intensity grows to become close to the intensity of Soret band. A similar changes were formerly marked in the spectrum of zinc *meso*-*cis*-diphenyltetrabenzodiazaporphyrinate [10]. Owing to unsymmetrical structure of the molecule of compound **X** the Soret band in its spectrum is split in two components of equal intensity, and the decrease in the dipole moment of the molecule leads to the disappearance of the charge transfer bands.

The electron absorption spectrum of complex **XI** (Fig. 2, 3) is similar in the character to the spectrum of zinc phthalocyaninate [11] and is distinguished by a small (5 nm) blue shift of Q band. Besides, a diffuse band of low intensity is observed in the region of 422 nm.

The analysis of the above data suggests a conclusion that the main factor governing the electronic structure of the synthesized metal complexes is the aza-substitution in the *meso*-positions of the porphyrin macroring. On the contrary, the *meso*-alkoxy substituents supplying the metal complexes with higher solubility in organic solvents do not considerably affect their electronic optical characteristics

EXPERIMENTAL

Electron absorption spectra of compounds obtained were measured on a spectrophotometer Hitachi UV-2001, ^1H NMR spectra in CDCl_3 (200 MHz, internal reference

HMDS), on a spectrometer Bruker AMD-200, IR spectra, on a spectrophotometer Avatar 360 FT-IR in the range 400–4000 cm^{-1} from films on a glass TlI_3 . Elemental analysis was performed on a FlashEA 1112 CHNS–O Analyzer.

1,3-Diiminoisoindoline (VI) was synthesized as described in [12].

Hexadecyloxyacetic acid (I). A mixture of 11.4 g (0.10 mol) of potassium glycolate, 39 g (0.11 mol) of 1-hexadecyl iodide, 41.4 g (0.30 mol) of K_2CO_3 , and 75 ml of DMF was heated to boiling at vigorous stirring for 5 h, then unreacted 1-hexadecyl iodide was removed by steam distillation. The reaction mixture was cooled, acidified with hydrochloric acid to pH 2, the precipitated acid I was filtered off, washed with 30 ml of cold water, and dried. Yield 11 g (37%), wax-like light-yellow substance. IR spectrum, ν , cm^{-1} : 2954, 2917, 2849, 1467 (C–H), 1731 (C=O), 1179, 1058 (C–O). ^1H NMR spectrum, δ , ppm: 10.55 s (1H), 4.05–3.92 d (2H), 3.65 t (2H), 2.16 s (2H), 1.24 s (26H), 0.85 s (3H). Found, %: C 70.88; H 12.33. $\text{C}_{18}\text{H}_{36}\text{O}_3$. Calculated, %: C 71.95; H 12.08.

Zinc meso-trans-di(hexadecyloxy)tetrabenzoporphyrinate (VII). A mixture of 1.3 g (4.8 mmol) of compound V, 1.6 g (5.3 mmol) of acid I, and 0.8 g of zinc oxide was heated at 300°C for 30 min, then it was cooled, extracted with chloroform and subjected to chromatography on a column packed with aluminum oxide of II grade of activity (eluent chloroform) ellecting the main green zone. Yield 0.37 g (15%), dark-green powder, well soluble in benzene, chloroform, acetone, tetrachloromethane. Electron absorption spectrum (CHCl_3), λ_{max} (D/D_{max}): 624 (0.33), 575 (0.19), 424 (1.00). ^1H NMR spectrum, δ , ppm: 9.13 s (2H), 7.80–7.30 m (16H), 4.01 t (4H), 2.17–2.11 m (4H), 1.19 s (52H), 0.87 s (6H). Found, %: C 77.67; H 8.12; N 4.62. $\text{C}_{68}\text{H}_{84}\text{N}_4\text{O}_2\text{Zn}$. Calculated, %: C 77.43; H 8.03; N 5.31.

Condensation of 1,3-diiminoisoindoline (VI) with hexadecyloxyacetic acid (I) in the presence of zinc oxide. A mixture of 1.5 g (10 mmol) of compound VI, 4.5 g (15 mmol) of acid I, and 1.5 g of zinc oxide was heated at 270°C for 45 min, then it was cooled, extracted with chloroform and subjected to chromatography on a column packed with aluminum oxide of II grade of activity (eluent a mixture of chloroform with acetone, 1:1 v/v) collecting the green zone. The solvent was removed, the residue was dissolved in toluene and subjected to repeated chromatography. On elution with toluene two green zones were separated, containing respectively

compounds II and VIII. On further elution with a mixture toluene–acetone–ethanol, 10:20:5 v/v, three additional blue-green zones were separated containing respectively compounds IX–XI. On removing the solvent we obtained compounds II, VIII–XI.

Zinc meso-tetra(hexadecyloxy)tetrabenzoporphyrinate (II). Yield 0.08 g (2%), wax-like green substance, well soluble in toluene, chloroform, tetrachloromethane, acetone. Electron absorption spectrum (CHCl_3), λ_{max} (D/D_{max}): 622 (0.37), 575 (0.06), 422 (1.00). ^1H NMR spectrum, δ , ppm: 7.74–7.29 m (16H), 4.08 t (8H), 2.15–2.13 m (8H), 1.21 s (104H), 0.87 s (12H). Found, %: C 78.75; H 9.91; N 3.07. $\text{C}_{100}\text{H}_{148}\text{N}_4\text{O}_4\text{Zn}$. Calculated, %: C 78.21; H 9.71; N 3.65.

Zinc meso-tri(hexadecyloxy)tetrabenzomonoazaporphyrinate (VIII). Yield 0.24 g (7%), wax-like green substance, well soluble in toluene, chloroform, tetrachloromethane, acetone. Electron absorption spectrum (CHCl_3), λ_{max} (D/D_{max}): 622 (0.62), 574 (0.09), 421 (1.00). ^1H NMR spectrum, δ , ppm: 7.77–7.31 m (16H), 4.09 t (6H), 2.14–2.12 m (6H), 1.21 s (78H), 0.85 s (9H). Found, %: C 77.17; H 9.44; N 4.92. $\text{C}_{83}\text{H}_{115}\text{N}_5\text{O}_3\text{Zn}$. Calculated, %: C 76.91; H 8.94; N 5.40.

Zinc meso-trans-di(hexadecyloxy)tetrabenzodiazaporphyrinate (IX). Yield 0.32 g (12%), blue-green powder, soluble in toluene, chloroform, tetrachloromethane, acetone. Electron absorption spectrum (CHCl_3), λ_{max} (D/D_{max}): 668 (0.38), 646 (0.22), 623 (0.32), 454 (0.23), 425 (1.00). ^1H NMR spectrum, δ , ppm: 7.79–7.35 m (16H), 4.07 t (4H), 2.10 s (4H), 1.22 s (52H), 0.87 s (6H). Found, %: C 75.87; H 8.01; N 7.12. $\text{C}_{66}\text{H}_{82}\text{N}_6\text{O}_2\text{Zn}$. Calculated, %: C 75.01; H 7.82; N 7.95.

Zinc meso-cis-di(hexadecyloxy)tetrabenzodiazaporphyrinate (X). Yield 0.19 g (7%), blue-green powder, soluble in toluene, chloroform, tetrachloromethane, acetone. Electron absorption spectrum (CHCl_3), λ_{max} (D/D_{max}): 662 (0.97), 574 (0.17), 424 (1.00), 418 (1.00), 397 (0.57). ^1H NMR spectrum, δ , ppm: 7.79–7.36 m (16H), 4.11 t (4H), 2.13 t (4H), 1.20 s (52H), 0.88 s (6H). Found, %: C 75.32; H 7.54; N 8.01. $\text{C}_{66}\text{H}_{82}\text{N}_6\text{O}_2\text{Zn}$. Calculated, %: C 75.01; H 7.82; N 7.95.

Zinc meso-mono(hexadecyloxy)tetrabenzotriazaporphyrinate (XI). Yield 0.08 g (4%), blue-green powder, soluble in toluene, chloroform, acetone. Electron absorption spectrum (CHCl_3), λ_{max} (D/D_{max}): 662 (1.00), 598 (0.26), 422 (0.41). ^1H NMR spectrum, δ , ppm: 7.82–7.55 m (16H), 4.10 t (2H), 2.08 t (2H), 1.25 s (26H), 0.87 s (3H). Found, %: C 71.77; H 5.72; N 12.16. $\text{C}_{49}\text{H}_{49}\text{N}_7\text{OZn}$. Calculated, %: C 72.01; H 6.04; N 12.00.

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