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5,15-Diaminotetrabenzoporphyrins: Synthesis and Spectral Properties

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Abstract—A zinc complex of 5,15-di(*N*-phthalimidyl)tetrabenzoporphyrin was obtained by the reaction of *N*-carboxymethylphthalimide with 1-oxo-1*H*-3-(1-oxoisoindolin-3-ylidenemethyl)isoindole and zinc oxide. The complex demetallation affords 5,15-di(*N*-phthalimidyl)tetrabenzoporphyrin. The reaction of *N*-phthalimidyl-substituted tetrabenzoporphyrins with hydrazine hydrate leads to the formation of 5,15-diaminotetrabenzoporphyrins. Spectral properties of these compounds were studied.

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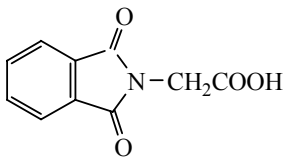
The interest of scientists and technologists in tthe unique group of porphyrin compounds, the *meso*-substituted tetrabenzoporphyrins, increases every year, probably due to the development of new, improved methods for their synthesis [1–3] ensuring the availability of these compounds for research and practical applications. The *meso*-substituted tetrabenzoporphyrins have been suggested as a material for the photodynamic cancer therapy [4, 5] and as catalysts [6].

Currently, *meso*-aryl- and *meso*-alkyl-substituted tetrabenzoporphyrins are the most studied. An information of tetrabenzoporphyrins containing in their *meso*-positions substituents of another nature, like nitro or amino groups, is rather limited, although they present no less theoretical and practical interest. This is due to the lack of convenient methods for obtaining such compounds. The known methods [7] of the synthesis of *meso*-nitro- and *meso*-amino-substituted tetrabenzoporphyrins, which consists in the synthesis of zinc tetrabenzoporphyrinate, its nitration with nitric acid in the medium of trifluoroacetic acid, and reduction of the nitro derivatives with tin metal in boiling acetic acid cannot be considered effective because of the multistage nature of the process, the low selectivity of the nitration and preparative complexity of the reduction of the nitro group.

In this paper, an attempt was made to develop a more convenient method of the synthesis of *meso*-amino-substituted tetrabenzoporphyrins.

Among the methods of obtaining the *meso*-substituted tetrabenzoporphyrins there is a template condensation of phthalimide with substituted acetic acid [8]. This one-step method is simple, but it has a major drawback: the low stability of many of substituted acetic acid derivatives at high temperatures. Thus, our attempts to synthesize *meso*-amino-substituted tetrabenzoporphyrins by the reaction of aminoacetic acid with phthalimide and zinc oxide were unsuccessful. When heating a mixture of the reactants to a temperature above 250°C tarring occurred, probably due to the processes of oxidation involving the primary amino groups.

In this regard, we implemented a reaction of phthalic anhydride with aminoacetic acid in DMF solution at boiling and synthesized in high yield N-carboxymethylphthalimide (**I**). Compound **I** is a light yellow crystalline substance, soluble in water, readily soluble in pyridine, DMSO and DMF, soluble in alkali with decomposition. Its composition and structure were confirmed by elemental analysis, IR and ^{1}H NMR spectroscopy.

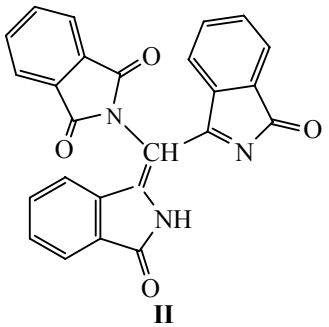


I

In the IR spectrum of compound **I** there is a strong band at 1718 cm^{-1}, characterizing the stretching C=O vibrations, the bands at 1419 and 1247 cm^{-1} correspond to the stretching vibrations of C=C bonds in the aromatic fragments, the bands at 2933 and 1467 cm^{-1} characterize the vibrations of C–H bonds of the methylene groups.

In the ^{1}H NMR spectrum of a solution of acid **I** in DMSO-d_6 (Fig. 1) there are two quadruplets in a weak field at 7.81–7.79 and 7.74–7.72 ppm corresponding to the resonance of the four protons of the benzene ring in 3, 6, and 4, 5 positions, respectively. In a strong field there is a singlet at 4.28 ppm, which characterizes the resonance of the two protons of the methylene group. The proton resonance of the carboxy group in the spectrum is not seen, probably due to the processes of deuterium exchange.

We have attempted to synthesise zinc 5,10,15,20-tetra(*N*-phthalimidyl)tetrabenzoporphyrinate by heating acid **I** with phthalimide in the presence of zinc oxide at different ratios of reactants and temperatures. However, the attempts failed, probably due to steric constraints to the formation of *meso*-tetra-substituted tetrabenzoporphyrins. The process ends mainly at the stage of the formation of 3,3'- [1-(1-oxo-1*H*-isoindol-3-yl)-(*N*-phthalimidyl)idene]-2,3-dihydro-1*H*-isoindole-1-one (**II**). This assumption is confirmed by the facts that the reaction mixture is colored to dark-red, and in its mass spectrum (electron impact ionization) there is a signal at *m*/*z* 419, corresponding to a molecular ion $[M]^+$ of compound **II** and the peaks of the products of its fragmentation, *m*/*z* 290, 274, and 160.



II

The effect of steric factors on the formation of 5,15-disubstituted tetrabenzoporphyrins is much smaller [9]. Therefore, for the synthesis of compounds of this structure, we used 3,3'-[1-(1-oxo-1*H*-isoindol-3-yl)methyl]-2,3-dihydro-1*H*-isoindol-1-one (**III**) obtained by the known procedure [10] through the condensation of phthalimide with zinc acetate.

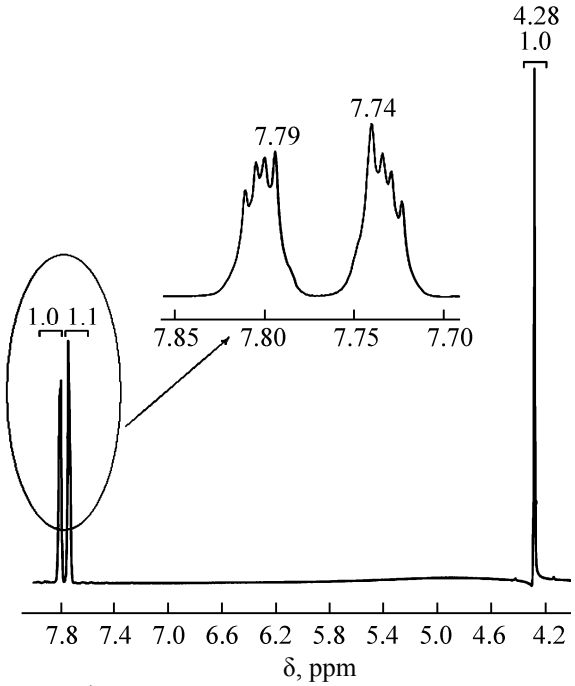


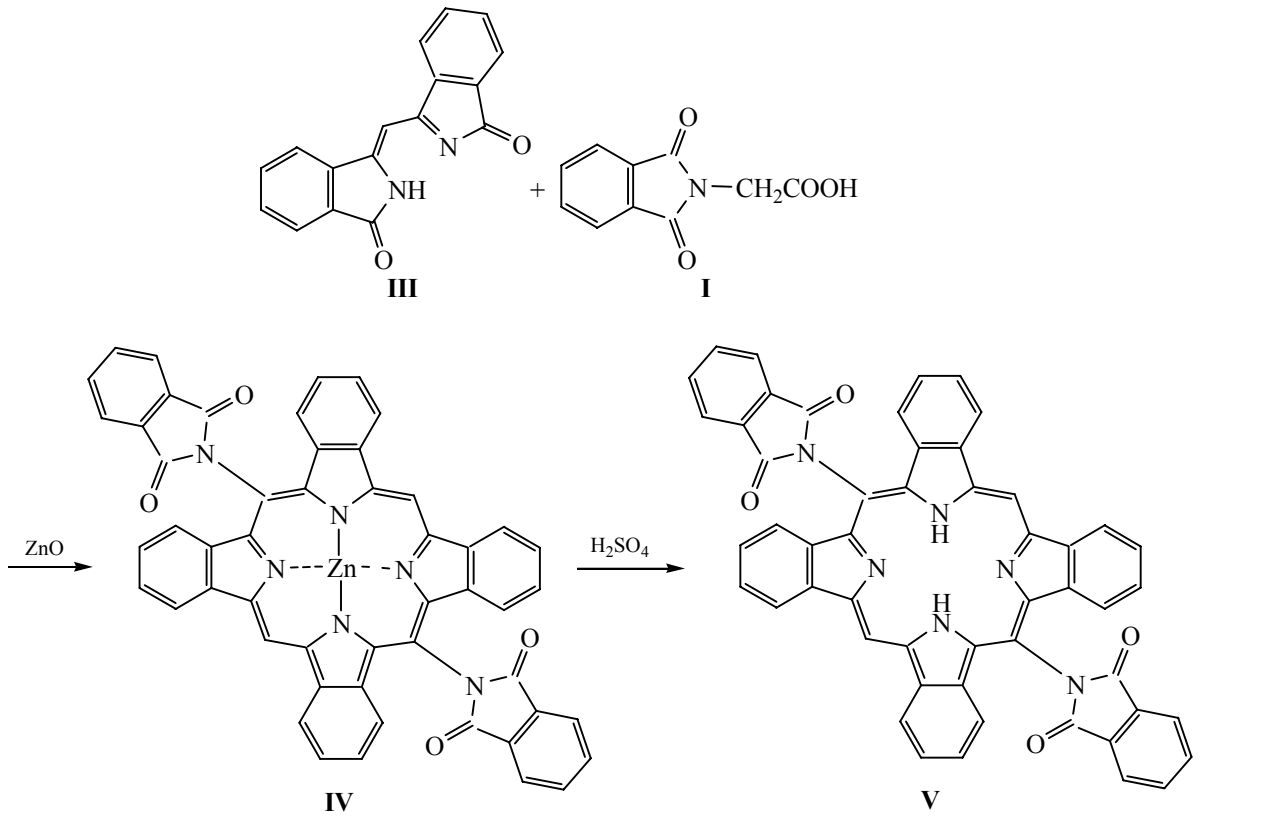
Fig. 1. ^{1}H NMR spectrum of compound **I** in DMSO-d_6.

The interaction of compound **III** with acid **I** in the presence of zinc oxide at 350°C over 50 min leads to the formation of zinc 5,15-di(*N*-phthalimidyl)tetrabenzoporphyrinate (**IV**) in a 32% yield, from which we obtained 5,15-di(*N*-phthalimidyl)tetrabenzoporphyrin (**V**) by the demetallation with concentrated sulfuric acid.

The porphyrins **IV** and **V** were purified by column chromatography on alumina using a chloroform–pyridine mixture as an eluent. The resulting compounds are dark green substances soluble in pyridine, DMF, DMSO, and insoluble in water. Their composition and structure were confirmed by elemental analysis, vibrational, electronic, and ^{1}H NMR spectroscopy.

The IR spectrum of complex **IV** contains a band at 3065 cm^{-1} belonging to CH stretching vibrations of aromatic fragments, the band at 1710 cm^{-1} characterizing the C=O stretching vibrations, and the bands at 1457 and 1295 cm^{-1} corresponding to C=C stretching vibrations in the aromatic fragments.

In the ^{1}H NMR spectrum of compound **IV** in the weakest fields there is a singlet at 10.51 ppm corresponding to the resonance of the two *meso*-proton. The multiplets at 9.61–9.55, 8.11–8.05 and 7.95–7.78 ppm correspond to the resonance of the sixteen protons of the macrocycle benzene rings, and the multiplets at 7.67–7.61 and 7.46–7.41 ppm characterize



the resonance of eight protons of the benzene rings of *meso*-substituents.

The ^{1}H NMR spectrum of porphyrin **V** is similar by the character and position of signals to the spectrum of complex **IV**, and differs mainly by the presence of a signal of two protons of the endocyclic imino groups at –1.98 ppm.

The electron absorption spectrum of compound **IV** (Fig. 2, curve *1*) contains strong bands at 629 and 434 nm in the visible region. The positions of these bands are close to the respective position in the spectrum of zinc tetrabenzoporphyrinate, indicating that there is no noticeable distortion of the porphyrin macrocycle. Apart from these, in the spectrum there are less intense bands at 493 and 697 nm which do not occur in the spectrum of zinc tetrabenzoporphyrinate, belonging to n–π* transitions involving the nonbonding orbitals of the nitrogen atoms of *meso*-substituents.

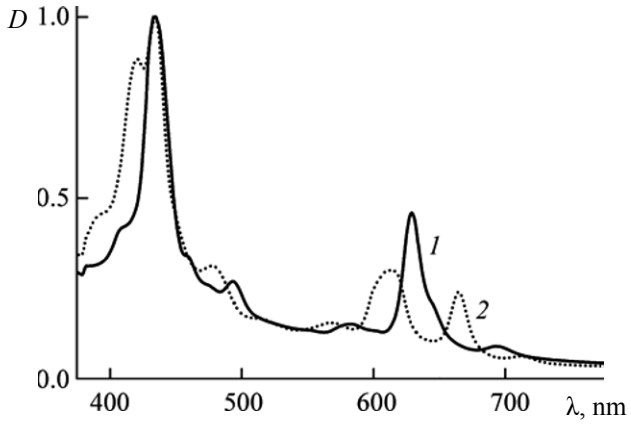
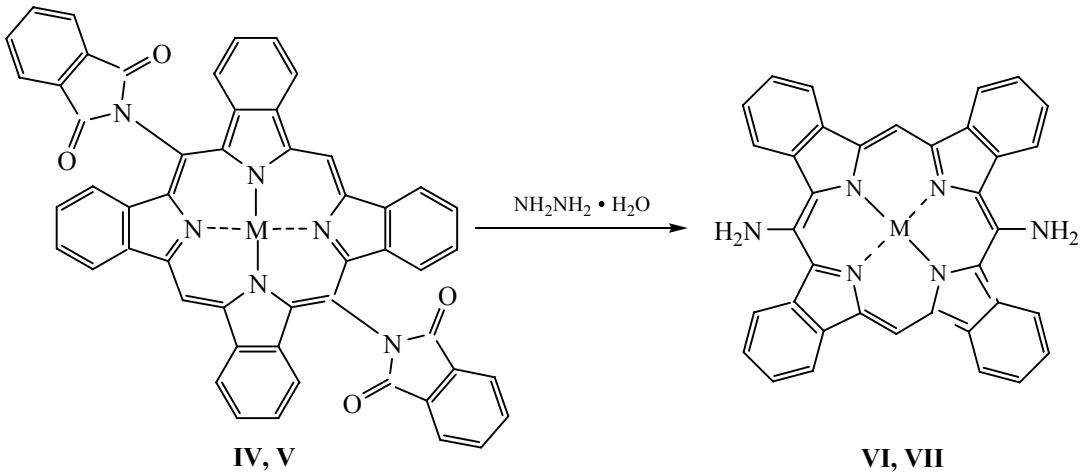


Fig. 2. Electron absorption spectra (solvent DMF): (*1*) compound **IV**, (*2*) compound **V.**

In the electron absorption spectrum of porphyrin **V** (Fig. 2, curve *2*) the absorption bands are also in the same areas as in the spectrum of the tetrabenzoporphyrin, and the bands at 478 and 716 nm correspond to n–π* transitions.

The synthesis of 5,15-diaminotetrabenzoporphyrins (**VI, VII**) was carried out by reacting compounds **IV** or **V** with hydrazine hydrate in pyridine medium at reflux for 3 h.

Compounds **VI** and **VII** were purified by column chromatography on silica gel C-60. In contrast to the unsubstituted tetrabenzoporphyrin and its zinc complex, and to porphyrins **IV** and **V**, they are readily soluble in low polarity solvents, which allowed the use of chloroform as an eluent. Porphyrins **VI** and **VII** are



IV, V **VI, VII**

M = Zn (**IV, VI**), 2H (**V, VII**).

crystalline compounds of dark green color, soluble in acetone, chloroform, benzene, sparingly soluble in the solutions of mineral acids, and insoluble in water. Their composition and structure were confirmed by elemental analysis and vibrational, electronic and ^{1}H NMR spectroscopy.

The IR spectra of complex **VI** and ligand **VII** contain the characteristic bands at 3322–3320 and 1596–1590 cm^{-1} of the stretching and bending vibrations of amino groups, respectively. The ^{1}H NMR spectrum of complex **VI** dissolved in $CDCl_3$ contains a singlet at 9.48 ppm in the weakest field, attributable to the resonance of two protons at the 10 and 20 positions of the macrocycle. Two singlets at 7.92 and 7.89 ppm characterize the resonance of four protons of two amino groups. Multiplets at 8.23, 7.54, and 7.49 ppm correspond to the resonance of sixteen protons of the benzene rings of the macrocycle. A significant downfield shift of the proton signals of amino groups is noteworthy. This is probably due to their strong deshielding because of the influence of the aromatic macrocycle. In the ^{1}H NMR spectrum of the ligand **VII** a broad singlet is present at –1.73 ppm, which characterizes the resonance of two protons of the endocyclic imino groups.

The electron absorption spectra of compounds **VI** and **VII** (Fig. 3) are similar to the spectra of porphyrins **IV** and **V** by the nature and position of the bands, and also contain the bands in the regions of 477–492 and 695–717 nm due to n–π* transitions involving the nonbonding orbitals of the nitrogen atoms of amino groups. It is noteworthy, however, that while the spectrum of porphyrin **IV** contains only a shoulder on the long-wavelength Q-band at 642 nm (Fig. 2, curve *1*), in the spectrum of complex **VI** (Fig. 3, curve *1*) a resolved band appears at 643 nm of the charge transfer from the electron-donor substituents on the macrocycle.

EXPERIMENTAL

The electron absorption spectra of the compounds obtained were measured on a Hitachi UV-2001 spectrophotometer. The ^{1}H NMR spectra were taken on a Bruker Avance-500 instrument (500 MHz), solvents DMSO-d_6 and $CDCl_3$, internal reference TMS. IR spectra were recorded on an Avatar 360 FT-IR spectrophotometer in the region 400–4000 cm^{-1} from thin films on the TlI glass. Mass spectra were recorded on a Varian Saturn 2000R GC-MS spectrometer. The elemental analysis was performed on a FlashEA 1112 CHNS-O Analyzer.

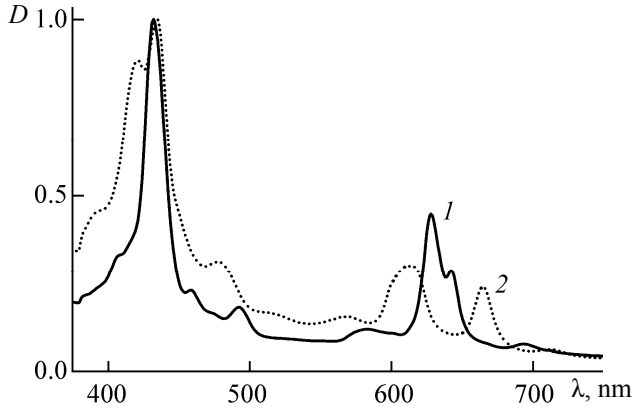


Fig. 3. The electron absorption spectra (solvent $CHCl_3$): (*1*) compound **VI**, (*2*) compound **VII.**

***N*-Carboxymethylphthalimide (I)**. A solution of 23.0 g (0.16 mol) of phthalic anhydride and 12.7 g (0.17 mol) of aminoacetic acid in 50 ml of DMF was heated at reflux for 6 h, then poured into 100 ml of water, the precipitate was filtered off, washed with 50 ml of water, and dried. Yield 6.30 g (96%). Pale yellow powder, poorly soluble in water, soluble in DMF, DMSO, and pyridine. IR spectrum, ν, cm^{-1}: 2933, 1467 (C–H), 1718 (C=O), 1419, 1247 (C=C), 738, 713 (C–C). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.81–7.79 q (2H, Ar; $J_{1,2}$ 2.84 Hz, $J_{1,3}$ 5.36 Hz, $J_{1,4}$ 8.20 Hz), 7.74 –7.72 q (2H, Ar; $J_{1,2}$ 3.16 Hz, $J_{1,3}$ 5.68 Hz, $J_{1,4}$ 8.51 Hz), 4.28 s (2H, CH_2). Found, %: C 59.12; N 6.73, H 3.88. $C_{10}H_7NO_4$. Calculated, %: C 58.54; N 6.83, H 3.44.

Zinc 5,15-Di(*N*-phthalimidyl)tetrabenzoporphyrinate (IV). A mixture of 3.0 g (0.011 mol) of compound **I**, 2.7 g (0.013 mol) of compound **III,** and 0.6 g of zinc oxide was heated to 350°C and maintained at this temperature for 50 min, then the reaction mixture was cooled, ground, suspended in 500 ml of 20% solution of Na_2CO_3, and kept at 90°C for 15 min. The precipitate was filtered off, washed with 200 ml of water, dried, and treated with butyl alcohol in a Soxhlet apparatus for 24 h. The residue was dissolved in pyridine and chromatographed on a column filled with aluminum oxide of II degree of activity (eluent a mixture of chloroform–pyridine, 1:1 by volume), collecting the main green area. Yield 2.2 g (32%), dark-green powder, soluble in pyridine, DMF, DMSO, poorly soluble in acetone, benzene, chloroform. IR spectrum, ν, cm^{-1}: 3065 (C–H), 1710 (C=O), 1457, 1295 (C=C), 1501, 1465 (C–N). The electron absorption spectrum (DMF), λ_{max}, nm (log ε): 410 (4.51), 434 (4.89), 459 (4.42), 493 (4.31) 583 (4.06), 629 (4.55), 697 (3.84). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 10.51 s (2H), 9.61 s (4H), 8.11–8.05 m (8H), 7.95–7.78 m (4H), 7.61–7.67 m (4H), 7.46–7.41 m (4H). Found, %: C 72.41; H 3.34; N 9.67. $C_{52}H_{26}NO_4Zn$. Calculated, %: C 72.27; H 3.03; N 9.72.

5,15-Di(*N*-phthalimidyl)tetrabenzoporphyrin (V). 1.0 g (0.0011 mol) of the metal complex **IV** was dissolved in 50 ml of sulfuric acid monohydrate and kept for 2 h at 20°C, then poured into 100 ml of water. The precipitate was filtered off and washed with 100 ml of 20% solution of ammonia, then 200 ml of water, and dried. The residue was dissolved in pyridine and chromatographed on alumina (eluent chloroform–pyridine, 1:1 by volume), collecting the main green area. Yield 0.79 g (85%), dark green powder, soluble in pyridine, DMF, DMSO, poorly soluble in acetone, benzene, chloroform. IR spectrum, ν, cm^{-1}: 3412 (N–H), 3063 (C–H_{Ar}), 1711 (C=O), 1458, 1296 (C=C_{Ar}), 1504, 1463 (C–N). The electron absorption spectrum (DMF), λ_{max}, nm (log ε): 392 (4.60), 421 (4.89), 435 (4.94), 478 (4.43), 516 (4.16) 567 (4.13), 612 (4.42) 665 (4.32) 712 (3.73). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 10.54 s (2H), 9.63 s (4H), 8.12–8.07 m (8H), 7.97–7.81 m (4H), 7.64–7.71 m (4H), 7.48–7.44 m (4H), –1.98 s (2H). Found, %: C 78.36; H 3.74; N 10.22. $C_{52}H_{28}NO_4$. Calculated, %: C 77.99; H 3.52; N 10.49.

Zinc 5,15-Diaminotetrabenzoporphyrinate (VI) and 5,15-diaminotetrabenzoporphyrin (VII). *General procedure*. 0.58 mmol of a compound **IV** or **V** was dissolved in 10 ml of pyridine, 2 ml of 70% hydrazine hydrate was added, and the mixture was heated at reflux for 3 h. Then the solvent was evaporated, the residue was dissolved in chloroform and chromatographed on silica gel C-60 (eluent chloroform), collecting the main green area.

Zinc *meso-trans*-diaminotetrabenzoporphyrinate (VI). Yield 0.3 g (86%), dark green powder, soluble in chloroform, acetone, toluene, pyridine, DMF, DMSO. IR spectrum, ν, cm^{-1}: 3320, 1590 (NH_2), 3060, 2930, 2850 (C–H), 1550, 1451 (C=C), 1548, 1465 (C–N). The electron absorption spectrum ($CHCl_3$), λ_{max}, nm (log ε): 407 (4.50), 433 (4.87), 459 (4.41), 492 (4.30), 579 (4.05), 629 (4.54), 643 (4.45), 695 (3.84). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 9.48 s (2H), 8.23 m (4H), 7.92 s (2H), 7.89 with (2H), 7.54 m (8H), 7.49 m (4H). Found, %: C 72.13; H 4.51; N 13.44. $C_{36}H_{22}N_6Zn$. Calculated, %: C 71.59; H 3.67; N 13.91.

***meso-trans*-Diaminotetrabenzoporphyrin (VII)**. Yield 0.25 g (83%), dark-green powder, soluble in chloroform, acetone, toluene, pyridine, DMF, DMSO. IR spectrum, n, cm^{-1}: 3322, 1596 (NH_2), 3065 (C–H), 1459, 1293 (C = C), 1549, 1465 (C–N). The electron absorption spectrum (CHCl 3), λ_{max}, nm (log ε): 389 (4.59), 419 (4.88), 433 (4.87) 477 (4.41), 515 (4.16), 567 (4.12), 609 (4.42), 663 (4.31), 717 (3.71). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 9.55 s (2H), 8.29 m (4H), 7.91 s (2H), 7.78 with (2H), 7.55 m (8H), 7.51 m (4H), –1.73 s (2H). Found, %: C 79.21; H 4.69; N 14.39. $C_{36}H_{24}N_6$. Calculated, %: C 79.98; H 4.47; N 15.54.

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