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Porphyrazines of Symmetric and Unsymmetrical Structure with Fused Fragments of 1,4-Bis(2-phenoxyethoxy)benzene and 5,6-Diphenylpyrazine. Synthesis and Spectral Characteristics

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Abstract—By alkylation of 3,6-dihydroxyphthalonitrile with 1-bromo-2-phenoxyethane 3,6-bis(2-phenoxyethoxy)phthalonitrile was obtained. A random condensation of the nitrile with 2,3-dicyano-5,6-diphenylpyrazine in 1-butanol in the presence of lithium 1-butanolate porphyrazines were synthesized of symmetric and unsymmetrical structure, and their spectral characteristics were investigated.

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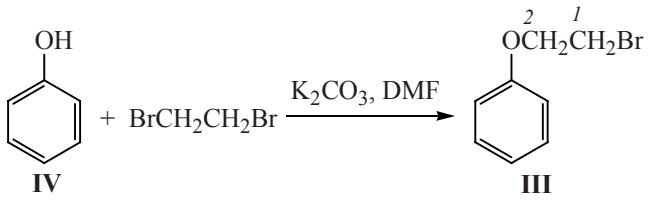
One of the most promising groups of tetrapyrrole macrocyclic compounds is the porphyrazines of unsymmetrical structure. Due to the presence of pronounced dipole moments these compounds are obviously interesting for application to the nonlinear optics [1–3], and the existing functional groups of various character make it possible to use the unsymmetrical porphyrazines in the medicine, in particular, for photodynamic therapy of the cancer diseases [4–7]. The synthesis of such porphyrazines most often consists in the random condensation of two different nitriles of aromatic *ortho*-dicarboxylic acids in the presence of a template agent [8–10]. As a result a mixture of all possible porphyrazines is obtained that according to the common classification belong to the following types: A_4, A_3B, AABB, ABAB, AB_3, and B_4, where A and B are various peripheral fragments in porphyrazine molecules. In contrast to symmetric porphyrazines their analogs of unsymmetrical structure are relatively poorly studied group because of the difficulties arising in their preparation, isolation, and purification.

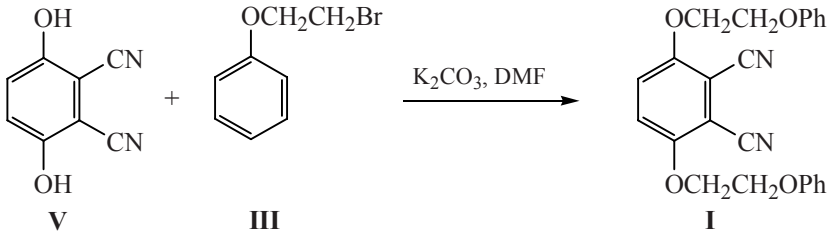
We report here on the random condensation of 3,6-bis(2-phenoxyethoxy)phthalonitrile (**I**) with 2,3-dicyano-5,6-diphenylpyrazine (**II**) in 1-butanol in the presence of lithium 1-butanolate affording porphyrazines of symmetric and unsymmetrical structure (A_4, A_3B, AABB, ABAB, AB_3), and also on the investigation of the spectral characteristics of compounds. The synthesis of compound **I** was performed from 1-bromo-2-phenoxyethane (**III**), obtained in its turn by the reaction of phenol (**IV**) with excess 1,2-dibromoethane in DMF in the presence of K_2CO_3.



IV **III**

Compound **III** is a viscous light-yellow fluid well soluble in organic solvents. Its composition and structure were confirmed by elemental analysis, vibrational and ^{1}H NMR spectra. In the IR spectrum of compound **III** the following absorption bands were observed: at 1125 and 1186 cm^{-1} ($\nu_{C–O–C}$), strong band at 2911 cm^{-1} ($\nu_{C–H}$), a band at 672 cm^{-1} ($\nu_{C–Br}$). In the ^{1}H NMR spectrum of compound **III** a multiplet appeared in the region 7.11–6.98 ppm corresponding to five protons of the benzene ring; the multiplet at 4.32 ppm belonged to two protons of the methylene group in the position *2*, and the multiplet at 3.68 ppm, to two protons of the methylene group in the position *1*.

Nitrile **I** was obtained by the reaction of compounds **III** with 3,6-dihydroxyphthalonitrile (**V**) in the presence of K_2CO_3 in DMF.



V **III** **I**

R = $PhOCH_2CH_2$

Compound **I** is a light-gray powder well soluble in organic solvents. Its composition and structure were confirmed by elemental analysis, vibrational spectra, ^1H NMR, and mass spectra. In the IR spectrum of nitrile **I** absorption bands were observed at 2232 ($\nu_{C\equiv N}$), 1127, and 1188 (ν_{C-O-C}), 2933 cm^{-1} (ν_{C-H}). The ^1H NMR spectrum of compound **I** contained a singlet at 7.82 ppm belonging to two protons in positions *4* and *5* of the phthalonitrile fragment; the multiplet in the region 7.01–6.82 ppm corresponded to the resonance of the 10 protons of the phenoxy groups, and the multiplet in the region 4.95–4.36 ppm originated from eight protons of the four methylene groups. In the mass spectrum of compound **I** (ionization by electron impact) peak of molecular ion, *m/z* 400 $[M]^+$, was observed, and also peaks of its fragmentation products: *m/z* 371 $[M - HCN]^+$, 320 $[M - Ph + 3]^+$ and 152 $[M - 2C_2H_4OPh + 6]^+$.

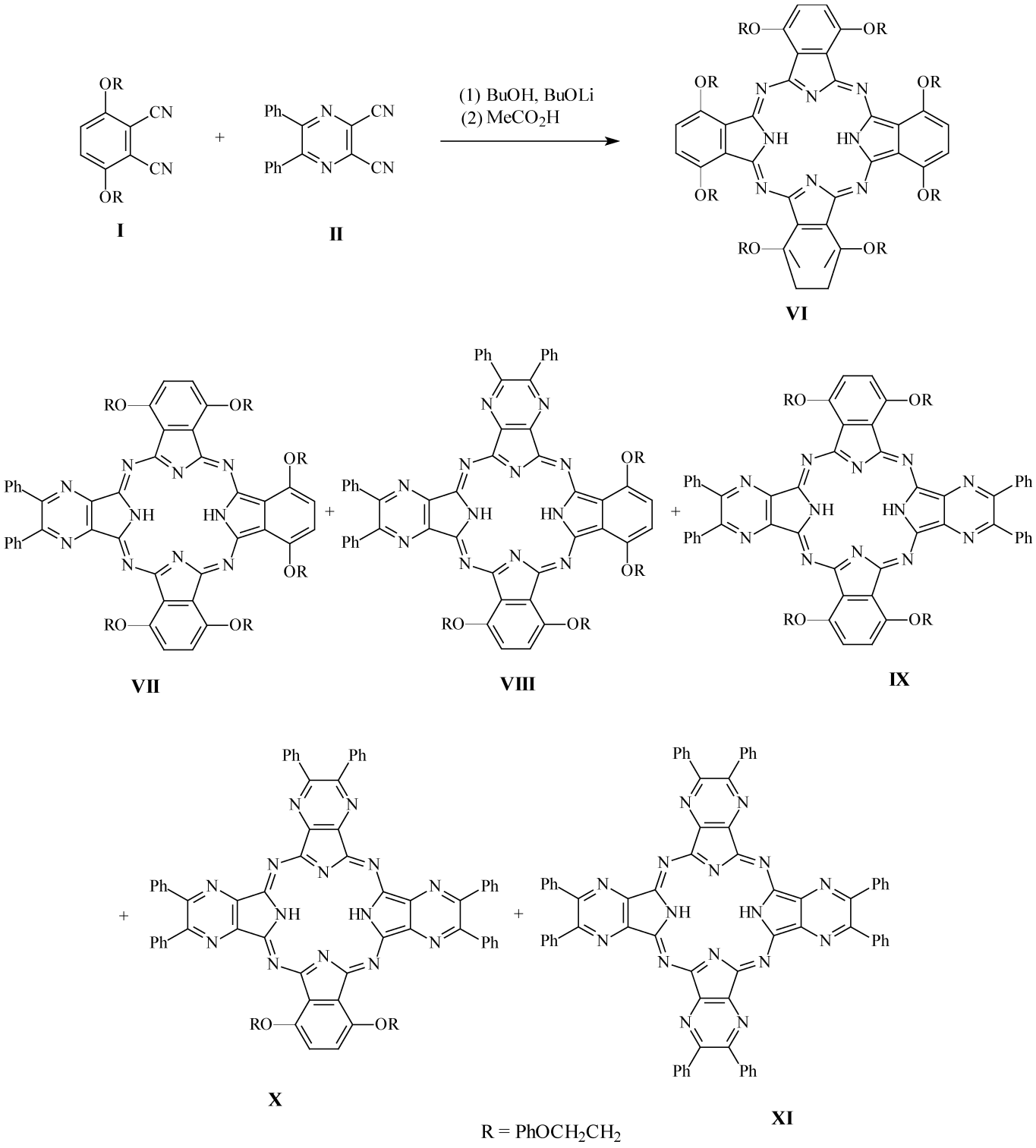
The heating of a mixture of nitrile **I** and 5,6-diphenylpyrazine-2,3-dicarbonitrile (**II**) prepared by procedure [11] in boiling 1-butanol in the presence of lithium 1-butanolate followed by the treatment with acetic acid resulted in the formation of a mixture of tetra[1,4-bis(2-phenoxyethoxy)benzo]porphyrazine (**VI**), tri[1,4-bis(2-phenoxyethoxy)benzo](5,6-diphenylpyrazino)porphyrazine (**VII**), *cis*-di[1,4-bis-(2-phenoxyethoxy)benzo]di(5,6-diphenylpyrazino)porphyrazine (**VIII**), *trans*-di[1,4-bis(2-phenoxyethoxy)benzo]di(5,6-diphenylpyrazino)-porphyrazine (**IX**), mono[1,4-bis(2-phenoxyethoxy)-benzo]tri(5,6-diphenylpyrazino)porphyrazine (**X**), and tetra-(5,6-diphenylpyrazino)porphyrazine (**XI**). From the mixture compounds **VI–X** were isolated by column chromatography.

Porphyrazines **VI–X** are green crystalline substances well soluble in benzene, chloroform, and acetone. Their composition and structure were confirmed by elemental analysis, ^1H NMR , and electronic spectra. The ^1H NMR spectrum of compound **VI** (A_4) in the region 7.22–7.13 ppm contained a multiplet corresponding to the eight protons of the benzene rings of the isoindole fragments, a multiplet in the region 7.09–6.98 ppm from the 40 protons of the eight phenoxy groups, and a multiplet in the region 4.58–4.33 ppm belonging to the 32 protons of the methylene groups of the eight phenoxyethoxy substituents. The signal from two protons of the endocyclic imino groups was observed at 0.26 ppm.

In the ^1H NMR spectrum of compound **VII** (A_3B) multiplets were observed from 10 protons of the phenyl substituents in the pyrazine fragments in the region 7.88–7.73 ppm, from six protons of benzene rings of the isoindole fragments in the region 7.28–7.21 ppm, from 30 protons of the six phenoxy groups in the region 7.10–7.01 ppm, and from 24 protons of the 12 methylene groups in the region 4.62–4.34 ppm. The signal from two protons of the endocyclic imino groups was shifted upfield to –0.3 ppm.

^1H NMR spectra of compounds **VIII–X** by their character and signals position resemble the spectrum of porphyrazine **VII** and differ mainly in the increase in the relative intensity of the proton signals of the phenyl substituents from the pyrazine fragments and in the decrease in the intensity of the methylene groups signals. Besides, with the growing number of the acceptor fragments of the diphenylpyrazine in the compounds series **VII > VIII**, **IX > X** the proton signals from the endocyclic imino groups shift upfield due to the growing aromaticity of porphyrazines in this series.

Electronic spectra of porphyrazines **VI–X** are characterized by a strong absorption in the (Q bands) and near UV region (B bands) (π–π^* transitions). In the electron absorption spectrum of compound **VI** (A_4) (Fig. 1, *1*) the Q band has a maximum at 737 nm; therewith like in the case of 3,6-octaalkoxyphthalocyanines [12, 13] the band is virtually nonsplit, only a small inflection is observed in the region 664 nm. As should be expected, the presence of eight phenoxyalkoxy substituents in the molecule of compound **VI** led to a significant (~40 nm) red shift of the longwave Q band as compared to its position in the spectrum of the



unsubstituted phthalo-cyanine. This shift is caused by a strong enhancement of the HOMO energy due to a significant contribution of the atomic orbitals of the carbon atoms in the positions *3* and *6* of isoindole fragments [14]. The B band has a maximum at 340 nm, and alongside this band in the spectrum of compound **VI** is a weak broadened band

In the electronic spectrum of porphyrazine **VII** (A_3B) (Fig. 1, *2*) the Q band is split in two components with the maxima at 713 and 693 nm, besides a shoulder is observed

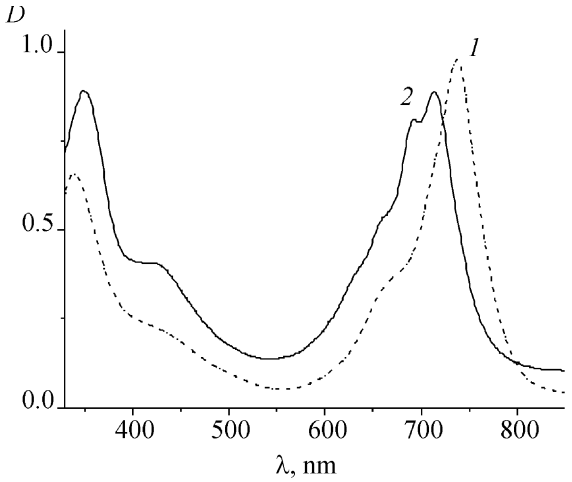


Fig. 1. Electron absorption spectra in $CHCl_3$ solution: (*1*) of compound **VI**, (*2*) of compound **VII**.

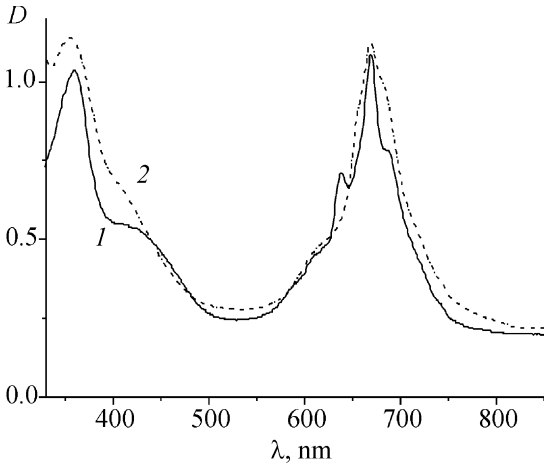


Fig. 2. Electron absorption spectra of compound **VIII**. (*1*) in $CHCl_3$, (*2*) in a mixture $CHCl_3$–$NHEt_2$.

in the region 657 nm. The three-band spectral character in the longwave region is one of the characteristic features of the metal-free porphyrazines A_3B; therewith the most longwave component of the Q-band as well as the band in the region 426 nm correspond to the charge transfer from the donor part of the molecule to the acceptor one [15].

In the electronic spectrum of compound **VIII** (AABB) (Fig. 2, *1*) the Q band is split in two components with the maxima at 669 and 638 nm, besides on its longwave wing an inflection is observed at 688 nm (charge transfer band). The B band suffers a red shift compared with its positions in the spectra of compounds **VI** and **VII** by 20 and 9 nm respectively due apparently to the increased dipole moment of compound **VIII**. Actually, according to the quantum-chemical calculations of molecules **VI–VIII** by

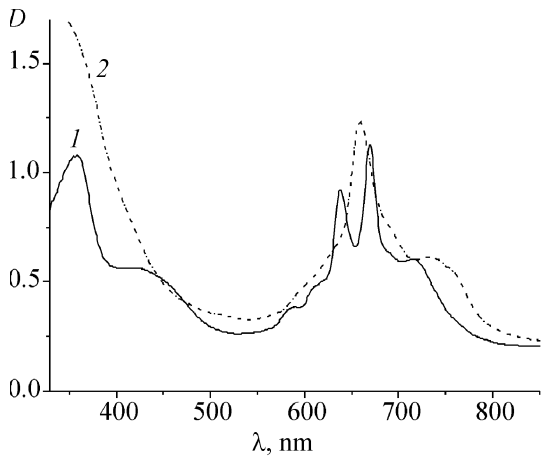


Fig. 3. Electron absorption spectra of compound **IX**. (*1*) in $CHCl_3$, (*2*) in a mixture $CHCl_3$–$NHEt_2$

the semiempirical method AM1 their dipole moments grew in the series 1.69, 4.64, and 5.03 D respectively supporting the above assumption.

The acidity of alkyl-substituted tetrapyrazinoporphyrazines is known to be considerably higher than that of phthalocyanine [16]. The increase in the number of electron-acceptor fragments in the molecules of porphyrazines **VII–X** also enhances their acidity, therefore on the addition of bases their electronic spectra should change because of the dianions formation. The addition of 10% of diethylamine to the solutions of compounds **VI** and **VII** in chloroform did not change the pattern of their electron absorption spectra due to their insufficient acidity. However the addition of 10% of diethylamine to the solution of compound **VIII** in chloroform resulted in the formation of its dianion, and in the electronic spectrum (Fig. 2, *2*) a decreased splitting of the Q band was observed due to the increased symmetry of the molecular orbitals, but the position of the maxima of the main absorption bands remained virtually unchanged.

The electron absorption spectrum of porphyrazine **IX** (ABAB) (Fig. 3, *1*) in its character and the maxima positions of the main absorption is analogous to the spectrum of bands compound **VIII**, but the intensity of the shortwave component of the Q band is enhanced in a good agreement with the four-orbital Gouterman model [17]. In the electron absorption spectrum of the dianion of compound **IX** (Fig. 3, *2*) two components of the Q band with the maxima at 669 and 639 nm merge into one band with a maximum at 660 nm, and the charge transfer band that in the spectrum of porphyrazine **IX** is observed in the region 718 nm suffers a red shift to 733 nm.

As to the electron absorption spectrum of porphyrazine **X** (AB_3) (Fig. 4, *1*), its Q band is split into two

components of equal intensity with the maxima at 667 and 640 nm. Note the considerable growth of the relative intensity of the B band. Whereas in the spectrum of porphyrazine **VII** (A_3B) the intensity ratio of Q and B bands is 1:1.01, in the spectrum of compound **X** (AB_3) it changes to 1:2.58. The reason of it is evidently the significant decrease in the energy of the vacant orbitals B_{3u} and B_{2u} under the effect of the electron-acceptor fragments of diphenylpyrazine. The electron absorption spectrum of the dianion of compound **X** (Fig. 4, *2*) contains a Q band with a maximum at 657 nm.

EXPERIMENTAL

Electron absorption spectra of compounds obtained were measured on a spectrophotometer Hitachi UV-2001, ^{1}H NMR spectra in $CDCl_3$ solution, on a spectrometer Bruker AMD-200 (200 MHz, internal reference TMS), IR spectra, on a spectrophotometer Avatar 360 FT-IR in the region 400–4000 cm^{-1} from thin films. Mass spectra were registered on a GC-MS instrument Varian Saturn 2000R. Elemental analysis was performed on a FlashEA 1112 CHNS–O Analyzer.

1-Brom*o*-2-phenoxyethane (III). A mixture of 3.1 g (0.03 mol) phenol (**IV**), 18.6 g (0.1 mol) of 1,2-dibromoethane, 7.0 g of K_2CO_3, and 40 ml of DMF was stirred at reflux for 8 h, then it was poured into 200 ml of water. The organic layer was separated, washed with 10% solution of HCl and water, then excess 1,2-dibromoethane was distilled off in a vacuum. The residue was subjected to column chromatography of alumina of the II grade of activity (eluent chloroform) collecting the light-yellow zone. Yield 4.5 g (67%), light-yellow viscous fluid, soluble in benzene, chloroform, acetone. IR spectrum, ν, cm^{-1}: 2911, 1524, 1401, 1186, 1125, 813, 672. ^{1}H NMR spectrum, δ, ppm: 7.11–6.98 m (5H), 4.32 m (2H), 3.68 m (2H). Found, %: C 47.79; H 4.51. C_8H_9BrO. Calculated, %: C 48.01; H 4.95.

3,6-Bis(2-phenoxyethoxy)phthalonitrile (I). A mixture of 2.0 g (10 mmol) of compound **III**, 0.8 g (5 mmol) of 3,6-dihydroxyphthalonitrile (**V**), 5.0 g of K_2CO_3, and 20 ml of DMF was stirred for 12 h at 120°C, then it was poured into 100 ml of water. The separated precipitate was filtered off, washed with water, with methanol, and dried. Yield 1.3 g (65%), light-gray powder, soluble in benzene, chloroform, acetone, sparingly soluble in methanol. IR spectrum, ν, cm^{-1}: 2933, 2232, 1529, 1403, 1188, 1127, 847. ^{1}H NMR spectrum, δ, ppm: 7.82 s (2H), 7.01–6.82 m (10H), 4.95–4.36 m (8H). Mass spectrum

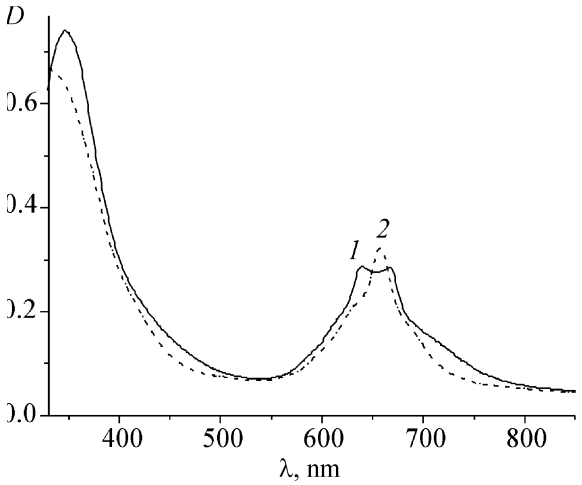


Fig. 4. Electron absorption spectra of compound **X**. (*1*) in $CHCl_3$, (*2*) in a mixture $CHCl_3$–$NHEt_2$

(electron impact, 70 eV), *m/z* (I_{rel}, %): 400 $[M]^+$ (12), 371 $[M - HCN]^+$ (10), 320 $[M - Ph + 3]^+$ (54), 152 $[M - 2C_2H_4OPh + 6]^+$ (100). Found, %: C 72.22; H 5.11; N 6.63.$C_{24}H_{20}N_2O_4$. Calculated, %: C 71.99; H 5.03; N 7.00.

Condensation of 3,6-bis(2-phenoxyethoxy)phthalonitrile (I) with 5,6-diphenylpyrazine-2,3-dicarbonitrile (II). Into a solution of lithium butanolate prepared by dissolving 0.2 g of lithium in 30 ml of anhydrous 1-butanol was charged 0.4 g (1.0 mmol) of compound **I**, 0.3 g (1.0 mmol) of compound **II**, and the mixture was refluxed for 3 h. The reaction mixture was cooled, 10 ml of acetic acid and 20 ml of water was added, the separated precipitate was filtered off, washed on the filter with 10 ml of methanol, and dried. The product was dissolved in benzene and was subjected to chromatography on a column packed with silica gel 60 (eluent benzene–chloroform–acetone, 50:20:1 by volume). The product divided into 5 zones. On removing the solvent compounds **VI–X** were obtained.

Tetra[1,4-bis(2-phenoxyethoxy)benzo]porphyrazine (VI) (A_4). Yield 0.04 g (10%), green powder, well soluble in benzene, chloroform, insoluble in water. Electron absorption spectrum ($CHCl_3$), λ_{max}, nm (D/D_{max}): 737 (1.00), 664 sh, 431 sh, 340 (0.67). ^{1}H NMR spectrum, δ, ppm: 7.22–7.13 m (8H), 7.09–6.98 m (40H), 4.58–4.33 m (32H), 0.26 s (2H). Found, %: C 72.02; H 5.61; N 6.13. $C_{96}H_{82}N_8O_{16}$. Calculated, %: C 71.90; H 5.15; N 6.99.

Tri[1,4-bis(2-phenoxyethoxy)benzo](5,6-diphenylpyrazino)porphyrazine (VII) (A_3B). Yield

0.06 g (12%), green powder, well soluble in benzene, chloroform, insoluble in water. Electron absorption spectrum ($CHCl_3$), λ_{max}, nm (D/D_{max}): 713 (0.94), 693 (0.91), 657 sh, 426 (0.45), 349 (1.00). ^{1}H NMR spectrum, δ, ppm: 7.88–7.73 m (10H), 7.28–7.21 m (6H), 7.10–7.01 m (30H), 4.62–4.34 m (24H), –0.31 s (2H). Found, %: C 72.88; H 5.01; N 9.16. $C_{90}H_{72}N_{10}O_{12}$. Calculated, %: C 72.76; H 4.88; N 9.43.

***cis*-Di[1,4-bis(2-phenoxyethoxy)benzo]di(5,6-diphenylpyrazino)porphyrazine (VIII) (AABB).** Yield 0.09 g (13%), green powder, well soluble in benzene, chloroform, insoluble in water. Electron absorption spectrum, λ_{max}, nm (D/D_{max}) in $CHCl_3$: 687 (0.72), 669 (1.00), 638 (0.65), 428 (0.49), 359 (0.95); in $CHCl_3$ + $NHEt_2$: 685 (0.85), 668 (0.98), 356 (1.00). ^{1}H NMR spectrum, δ, ppm: 7.89–7.75 m (20H), 7.27–7.21 m (4H), 7.12–7.07 m (20H), 4.58–4.36 m (16H), –0.73 s (2H). Found, %: C 74.13; H 4.88; N 11.99. $C_{86}H_{62}N_{12}O_8$. Calculated, %: C 73.78; H 4.57; N 12.29.

***trans*-Di[1,4-bis(2-phenoxyethoxy)benzo]di-(5,6-diphenylpyrazino)porphyrazine (IX) (ABAB).** Yield 0.07 g (10%), green powder, well soluble in benzene, chloroform, insoluble in water. Electron absorption spectrum, λ_{max}, nm (D/D_{max}) in $CHCl_3$: 718 (0.53), 669 (1.00), 638 (0.82), 609 (0.42), 590 (0.34), 427 (0.50), 358 (0.96); in $CHCl_3$ + $NHEt_2$: 741 (0.35), 659 (0.71), 625 sh, 345 (1.00). ^{1}H NMR spectrum, δ, ppm: 7.88–7.73 m (20H), 7.29–7.22 m (4H), 7.12–7.10 m (20H), 4.58–4.48 m (16H), –0.75 s (2H). Found, %: C 74.33; H 4.49; N 11.71. $C_{86}H_{62}N_{12}O_8$. Calculated, %: C 73.78; H 4.57; N 12.29.

Mono[1,4-bis(2-phenoxyethoxy)benzo]tri(5,6-diphenylpyrazino)porphyrazine (X) (AB_3). Yield 0.14 g (11%), green powder, well soluble in benzene, chloroform, insoluble in water. Electron absorption spectrum, λ_{max}, nm (D/D_{max}) in $CHCl_3$: 667 (0.39), 641 (0.39), 347 (1.00); in $CHCl_3$ + $NHEt_2$: 657 (0.48), 631 sh, 331 (1.00). ^{1}H NMR spectrum, δ, ppm: 7.92–7.82 m (30H), 7.29–7.23 m (2H), 7.14–7.11 m (10H), 4.55–4.48 m (8H), –1.88 s (2H). Found, %: C 75.04; H 4.33; N 15.44. $C_{78}H_{52}N_{14}O_4$. Calculated, %: C 74.99; H 4.20; N 15.70.

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