

Synthesis and Isolation of 2,9,17,23–Tetrakis[(3,5–dimethyl–1H–pyrazol–1–yl)phenoxy]phthalocyanine and Its Magnesium(II) and Zinc(II) Complexes

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The synthesis of novel phthalocyanine containing four (3,5-dimethyl-1H-pyrazol-1-yl)phenoxy groups and its complexes with magnesium and zinc is reported. The practically pure C_s regioisomers of peripheral substituted phthalocyanines were separated and isolated by column chromatography with good yields. The structure and symmetry of synthesized phthalocyanines were confirmed by ¹H NMR, ¹³C NMR, IR, UV-Vis, and MS spectral data. Influence of metals and reaction conditions on the isolation of practically pure C_s regioisomers were discussed. Aggregation properties of phthalocyanines were investigated in DMF in different concentration ranges.

Keywords: Phthalocyanine, pyrazole, C_s regioisomer, isolation, aggregation.

Синтез и выделение 2,9,17,23–тетракис[(3,5–диметил–1H–пиразол–1–ил)фенокси]фталоцианина и его комплексов с магнием(II) и цинком(II)

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Работа посвящена синтезу нового фталоцианина, содержащего четыре (3,5-диметил-1H-пиразол-1-ил) фенокси группы, и его комплексов с магнием и цинком. Показано, что выделение практически чистых, индивидуальных C_s региоизомеров периферийно замещенных фталоцианинов с хорошими выходами неожиданно легко осуществляется при помощи простой колоночной хроматографии. Структура и симметрия синтезированных фталоцианинов подтверждалась данными ЯМР ¹H, ¹³C, ИК-, УФ-спектроскопии и масс-спектрометрии. Рассмотрено влияние природы металла, реакционных условий и методов очистки на выделение практически чистых C_s региоизомеров. Агрегационные свойства синтезированных фталоцианинов были исследованы в ДМФА в различных концентрационных диапазонах.

Ключевые слова: Фталоцианин, пиразол, C_s региоизомер, выделение, агрегация.

Introduction

Phthalocyanines are used as traditional dyes and pigments,^[1,2] and, thanks to the unique physical and chemical properties, as photocatalysts,^[3] semiconductor materials,^[4,5] photosensitizers for photodynamic therapy of cancer,^[6-10] materials of optoelectronics.^[11]

Substituted zinc and magnesium phthalocyanines have intensive red-visible region absorption with high extinction coefficient, both high singlet and triplet quantum yields and high singlet oxygen quantum yields. These properties make them important candidates as potential agents for fluorescence imaging and photodynamic therapy of cancer.^[12-16]

Unsubstituted phthalocyanines are known to have low solubility in most organic solvents that restricts of their application. Introduction of aryl or heteroaryl substituents in phthalocyanine core enhances solubility of macroheterocycles in many organic solvents and gives them new functional properties.

In the last decade intensive increase of number of the papers devoted to phthalocyanines, containing various nitrogen heterocycles is observed.^[17-27] These substituted phthalocyanines can be highly efficient photosensitizers of singlet oxygen due to dual or synergistic therapeutic effect.^[28,29] However, only a few works devoted to phthalocyanines^[30-32] and porphyrin^[33] containing pyrazole substituents are known. Interest to such substituents is caused by various biological activity of the pyrazole derivatives (antimicrobial,^[34] antipyretic,^[35] analgesic,^[36] anti-inflammatory,^[37] antiviral^[38] and other properties^[39]). The high singlet oxygen quantum yield of zinc phthalocyanine containing four 3,5-dimethylpyrazole-1-methoxy groups gives an indication of the potential of the zinc phthalocyanine as photosensitizer in photocatalytic applications such as PDT.^[31] However, phthalocyanines containing 3,5-dimethylpyrazole-1-phenoxy groups and their spectral properties are unknown practically.

The tetramerisation of 4-substituted phthalonitriles usually leads to a mixture of four regioisomers with expected statistical ratio of 1:1:2:4 for regioisomers with molecular symmetry as C_{4h} , D_{2h} , C_{2v} and C_s , respectively. The separation of the mixture of the four regioisomers by column chromatography is highly challenging^[40] and was achieved by preparative thin layer chromatography or HPLC with chiral column.^[41-46] It is known that due to the presence of bulky substituents, a pure regioisomer of 3-substituted ZnPc can be isolated by column chromatography. So, the one C_{4h} isomer of non-peripheral 3-(alkylaryloxy)-tetrasubstituted phthalocyanine was isolated by column chromatography in high yield.^[47] Moreover, it was shown that the photophysical, photochemical and photobiological properties of regioisomers were different and C_s regioisomer possessed a more effective action on cell death.^[45]

Recently^[48] we have published a paper dealing with the synthesis and isolation of C_s regioisomer zinc 2,9,17,23-tetrakis[(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy]-phthalocyanine by cyclotetramerization of 4-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy)phthalonitrile^[49] and zinc acetate with DBU in 1-pentanol.

This paper is devoted to the two methods of synthesis of 2,9,17,23-tetrakis[(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy]-phthalocyanine **2**, its magnesium complex **3** from phthalonitrile **1** and zinc complex **4** from phthalocyanine ligand **2** and isolation of practically pure C_s regioisomers. Influence of metals and reaction condition on the separation of C_s regioisomers is discussed. Spectral properties of the synthesized phthalocyanines in DMF also have been studied.

nitrite **1** and zinc complex **4** from phthalocyanine ligand **2** and isolation of practically pure C_s regioisomers. Influence of metals and reaction condition on the separation of C_s regioisomers is discussed. Spectral properties of the synthesized phthalocyanines in DMF also have been studied.

Experimental

All the reactions were carried out with dry, freshly distilled solvents. 4-(4-(3,5-Dimethyl-1H-pyrazol-1-yl)phenoxy)phthalonitrile (**1**) was synthesized using known procedure.^[49] The individuality of the products was monitored by thin layer chromatography (TLC) on Silufol UV-254 plates and compounds were visualized by exposure to UV light. All synthesized phthalocyanines **2-4** were purified by column chromatography at first column on Al_2O_3 (Sigma-Aldrich) using chloroform as an eluent, second column on Al_2O_3 with mixture THF:hexane:TEA:ethanol (25:75:1:5) as eluent and third column on a silica gel (Kieselgel, Hochrein, 60–200 mesh, Acros organics) with mixture $CHCl_3$:EtOH (50:1) as an eluent. The 1H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE 400 MHz spectrometer using $DMSO-d_6$ as the solvent. The chemical shifts are expressed in δ , ppm. The IR spectra were recorded in the range 4000–400 cm^{-1} as KBr pellets on a FTIR FSM 2202 spectrometer. The mass spectra were measured with a Bruker Daltonics MaXis mass spectrometer with electrospray ionization (ESI-QTOF) source. Absorption spectra in the UV-Vis region were recorded with a LOMO SF-2000 UV/Vis spectrophotometer.

Synthesis of magnesium 2,9,17,23-tetrakis[(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy]phthalocyanine, 3. The mixture of 4-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy)phthalonitrile (**1**) (0.300 g, 0.955 mmol), 1-pentanol (2 ml), and anhydrous $Mg(CH_3COO)_2$ (0.068 g, 0.477 mmol) was added into a single-necked flask and heated to the boiling point. After 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.25 ml) was added the mixture was stirred at reflux for 10 h, cooled, and diluted with *n*-hexane (50 ml). The precipitated solid was filtered, washed with hot *n*-hexane, and dried in air. The resulting product was purified by column chromatography to give dark green product. Yield 0.137 g (44 % on phthalonitrile **1**). IR cm^{-1} : 3060 (ν_{C-H} (arom.)), 2916 (ν_{C-H} (alk.)), 2864 (ν_{C-H} (alk.)), 1603 ($\nu_{C=C}$), 1555 ($\nu_{C=C}$), 1511 ($\nu_{C=N}$), 1482 ($\nu_{isoindole}$), 1470 ($\nu_{isoindole}$), 1389 ($\nu_{pyrazole}$), 1366 ($\nu_{pyrazole}$), 1335 ($\nu_{pyrrole}$ and Nmeso), 1231 ($\nu(C_{Ar}-O-C_{Ar})$), 1114 ($\delta_{isoindole}$), 1081 ($\delta(C_{Ar}-O-C_{Ar})$), 1044 (δ_{C-H}), 890 (δ_{C-H}), 833 (δ_{C-H}), 753 (δ (Pc rings)). 1H NMR ($[D_6]DMSO$) δ_H ppm: 2.22 s (3H, CH_3), 2.23 s (3H, CH_3), 2.24 s (3H, CH_3), 2.25 s (3H, CH_3), 2.35 s (3H, CH_3), 2.36 s (3H, CH_3), 2.42 s (3H, CH_3), 2.43 s (3H, CH_3), 6.09 s (1H, H_{pz}), 6.10 s (1H, H_{pz}), 6.12 s (1H, H_{pz}), 6.13 s (1H, H_{pz}), 7.47–7.54 m (4H, H_{ph}), 7.55–7.61 m (4H, H_{ph}), 7.63–7.68 m (4H, H_{ph}), 7.69–7.77 m (4H, H_{ph}), 7.81–7.91 m (4H, H_{ph}), 8.61–8.73 m (4H, H_a), 9.03–9.19 m (4H, H_a). ^{13}C NMR ($[D_6]DMSO$) δ_C ppm: 12.52–12.66, 13.79, 107.40–107.52, 111.53–112.24, 119.83–121.04, 124.54, 126.66, 133.96, 136.06–136.27, 139.66–139.73, 148.21–148.29, 151.76–152.55, 156.04–156.37, 158.29–158.61. MS (ESI) m/z : calculated for $C_{76}H_{57}N_{16}O_4Mg$: 1281.4594; found: 1281.4593 [$M+H^+$]. UV-Vis (DMF) λ_{max} nm (lge): 353 (4.91), 610 (4.53), 680 (5.25).

Synthesis of 2,9,17,23-tetrakis[(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy]phthalocyanine, 2. Method 1 (from phthalonitrile 1). The mixture of phthalonitrile **1** (0.100 g, 0.318 mmol) and 1-pentanol (2 ml) was added into a single-necked flask and heated to the boiling point. After DBU (0.25 ml) was added the mixture was stirred at reflux for 10 h, cooled, and diluted with *n*-hexane (30 ml). The precipitated solid was filtered and then washed with hot *n*-hexane and dried in air. The resulting product was purified by column chromatography to give dark green product. Yield 0.026 g (26 % on phthalonitrile **1**). **Method 2 (from magnesium complex 3).** The mixture of magnesium phthalocyanine **3** (0.1 g, 0.078 mmol) and

acetic acid (5 ml) was added into a single-necked flask and heated to 35 °C. After concentrated hydrochloric acid (1 ml) was added the mixture was stirred at 35 °C for 1 h, neutralized by NH_4OH , and product was extracted by chloroform. The resulting product was purified by column chromatography to give dark green product. Yield 0.070 g (71 % on phthalocyanine **3**). IR cm^{-1} : 3291 ($\nu_{\text{N-H}}$), 3065 ($\nu_{\text{C-H}}$ (arom.)), 2923 ($\nu_{\text{C-H}}$ (alk.)), 2858 ($\nu_{\text{C-H}}$ (alk.)), 1603 ($\nu_{\text{C=C}}$), 1556 ($\nu_{\text{C=C}}$), 1512 ($\nu_{\text{C=N}}$), 1475 ($\nu_{\text{isoindole}}$), 1383 (ν_{pyrazole}), 1366 (ν_{pyrazole}), 1338 ($\nu_{\text{pyrrole and N meso}}$), 1234 ($\nu(\text{C}_{\text{Ar}}-\text{O}-\text{C}_{\text{Ar}})$), 1113 ($\delta_{\text{isoindole}}$), 1092 ($\delta(\text{C}_{\text{Ar}}-\text{O}-\text{C}_{\text{Ar}})$), 1037 ($\delta_{\text{C-H}}$), 1009 ($\delta_{\text{N-H}}$), 884 ($\delta_{\text{C-H}}$), 834 ($\delta_{\text{C-H}}$), 747 ($\delta(\text{Pc rings})$). ^1H NMR ($[\text{D}_6]\text{DMSO}$) δ_{H} ppm: 2.19 s (12H, CH_3), 2.33 s (12H, CH_3), 6.07 s (4H, H_{pz}), 7.15–7.67 m (28H). MS (ESI) m/z : calculated for $\text{C}_{76}\text{H}_{59}\text{N}_{16}\text{O}_4$: 1259.4900; found: 1259.4897 [$\text{M}+\text{H}^+$]. UV-Vis (DMF) λ_{max} nm (lge): 342 (5.00), 605 (4.67), 635 (4.83), 667 (5.11), 698 (5.18).

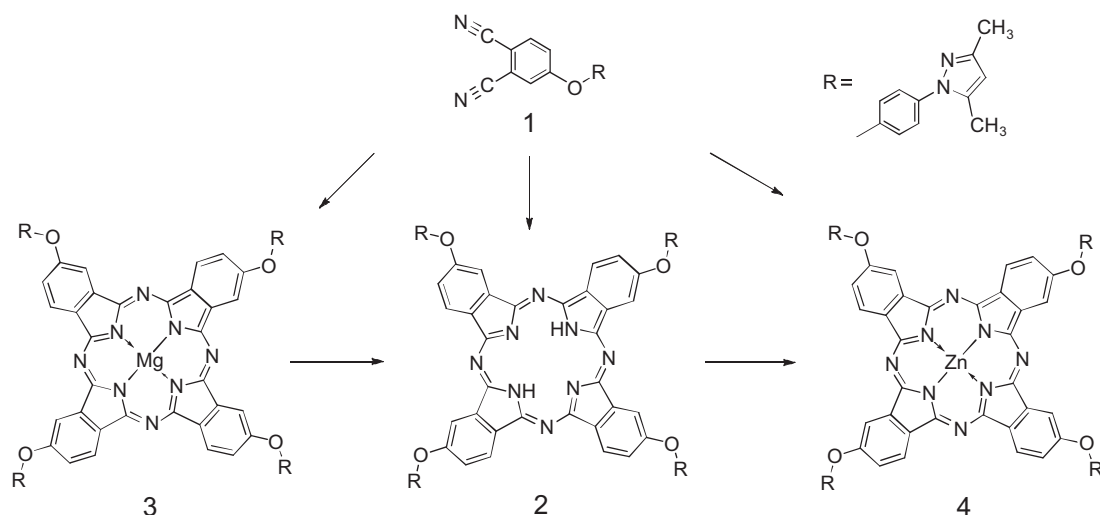
Synthesis of zinc 2,9,17,23-tetrakis[(3,5-dimethyl-1H-pyrazol-1-yl)phenoxy]phthalocyanine, **4. Method 1^[48] (from phthalonitrile **1**).** The mixture of phthalonitrile **1** (0.100 g, 0.318 mmol), 1-pentanol (2 ml), and anhydrous $\text{Zn}(\text{CH}_3\text{COO})_2$ (0.013 g, 0.080 mmol) was added into a single-necked flask and heated to the boiling point. After DBU (0.25 ml) was added the mixture was stirred at reflux for 10 h, cooled, and diluted with *n*-hexane (30 ml). The precipitated solid was filtered and then washed with hot *n*-hexane and dried in air. The resulting product was purified by column chromatography to give dark green product. Yield 0.062 g (59 % on phthalonitrile **1**). **Method 2 (from phthalocyanine **2**).** The mixture of phthalocyanine **2** (0.050 g, 0.039 mmol), anhydrous $\text{Zn}(\text{CH}_3\text{COO})_2$ (0.013 g, 0.080 mmol), and DMF (5 ml) was added into a single-necked flask and stirred at 130 °C for 1 h. Then the mixture was cooled and diluted with water (25 ml). The precipitated solid was centrifuged and dried in air. The resulting product was purified by column chromatography to give dark green product. Yield 0.040 g (80 % on phthalocyanine **2**). IR cm^{-1} : 3067 ($\nu_{\text{C-H}}$ (arom.)), 2920 ($\nu_{\text{C-H}}$ (alk.)), 2846 ($\nu_{\text{C-H}}$ (alk.)), 1603 ($\nu_{\text{C=C}}$), 1555 ($\nu_{\text{C=C}}$), 1511 ($\nu_{\text{C=N}}$), 1486 ($\nu_{\text{isoindole}}$), 1469 ($\nu_{\text{isoindole}}$), 1393 (ν_{pyrazole}), 1366 (ν_{pyrazole}), 1335 ($\nu_{\text{pyrrole and N meso}}$), 1232 ($\nu(\text{C}_{\text{Ar}}-\text{O}-\text{C}_{\text{Ar}})$), 1116 ($\delta_{\text{isoindole}}$), 1089 ($\delta(\text{C}_{\text{Ar}}-\text{O}-\text{C}_{\text{Ar}})$), 1043 ($\delta_{\text{C-H}}$), 891 ($\delta_{\text{C-H}}$), 833 ($\delta_{\text{C-H}}$), 748 ($\delta(\text{Pc rings})$). ^1H NMR ($[\text{D}_6]\text{DMSO}$) δ_{H} ppm: 2.23 s (3H, CH_3), 2.24 s (3H, CH_3), 2.25 s (3H, CH_3), 2.26 s (3H, CH_3), 2.36 s (3H, CH_3), 2.38 s (3H, CH_3), 2.43 s (3H, CH_3), 2.45 s (3H, CH_3), 6.01 s (1H, H_{pz}), 6.02 s (1H, H_{pz}), 6.04 s (1H, H_{pz}), 6.05 s (1H, H_{pz}), 7.44–7.48 m (4H, H_{ph}), 7.50–7.54 m (4H, H_{ph}), 7.59–7.63 m (4H, H_{ph}), 7.65–7.69 m (4H, H_{ph}), 7.82–7.89 m (4H, H_{p}), 8.77–8.81 m (4H, H_{a}), 9.13–9.23 m (4H, H_{a}). ^{13}C NMR ($[\text{D}_6]\text{DMSO}$) δ_{C} ppm: 12.66, 13.80, 107.48, 119.90–12.46, 126.67, 133.29, 136.09–136.31, 139.74, 148.30, 151.22, 156.06–156.29, 158.19–158.68. MS (ESI) m/z : calculated for $\text{C}_{76}\text{H}_{57}\text{N}_{16}\text{O}_4\text{Zn}$: 1321.4034; found: 1321.3997 [$\text{M}+\text{H}^+$]. UV-Vis (DMF) λ_{max} nm (lge): 357 (4.80), 611 (4.51), 678 (5.24).

Results and Discussion

The reaction pathways for the preparation of the metal-free phthalocyanine **2** and its complexes with magnesium **3** and zinc **4** are shown in Scheme 1. The magnesium phthalocyanine **3** and zinc phthalocyanine **4** were prepared by cyclotetramerization of known phthalonitrile **1**^[49] in the presence of anhydrous acetate salts of metals using DBU as the catalyst in 1-pentanol under reflux for 10 h as described for the last in work.^[48] Metal-free phthalocyanine **2** was synthesized by two different methods. The first method consisted in cyclotetramerization of phthalonitrile **1** in 1-pentanol in the presence of DBU, and the second – by a demetalation of magnesium phthalocyanine **3** in acetic acid with a catalytic amount of hydrochloric acid. Besides, zinc phthalocyanine **4** was prepared by reaction of complexation of zinc acetate and phthalocyanine ligand **2**, synthesized both from phthalonitrile **1** and from magnesium phthalocyanine **3**.

Condensation of 4-substituted phthalonitriles usually gives statistical mixture of regioisomers of peripheral tetrasubstituted phthalocyanines. This mixture is usually purified by a column chromatography, but most often isn't possible to isolate of individual regioisomers.

According to Scheme 2, the peripheral tetrasubstituted metal phthalocyanines have four different regioisomers with molecular symmetry as C_{4h} , D_{2h} , C_{2v} and C_s with statistical distribution of 12.5 %, 12.5 %, 25 % and 50 %, respectively. The symmetry of regioisomer can be determined by the number of signals in ^1H NMR spectrum.^[43–45] In the case C_{4h} and D_{2h} regioisomers all isoindole fragments with substituents R (A, B, C, D) are magnetically equivalent and the ^1H NMR spectra of these regioisomers must be similar to spectrum of corresponding substituted phthalonitrile. The C_{2v} regioisomer contains magnetically equivalent (A, D) and (B, C) pairs of isoindole fragments but these pairs are magnetically nonequivalent among themselves and ^1H NMR spectrum of this regioisomer must contain two signals with equal intensity of each proton of isoindole fragments with substituent R. In the case of C_s regioisomer all isoindole fragments with substituent R (A, B, C, D) are magnetically nonequivalent and ^1H NMR spectrum of this regioisomer



Scheme 1. The reaction pathways for preparation of metal-free phthalocyanine **2** and its complexes with magnesium **3** and zinc **4**.

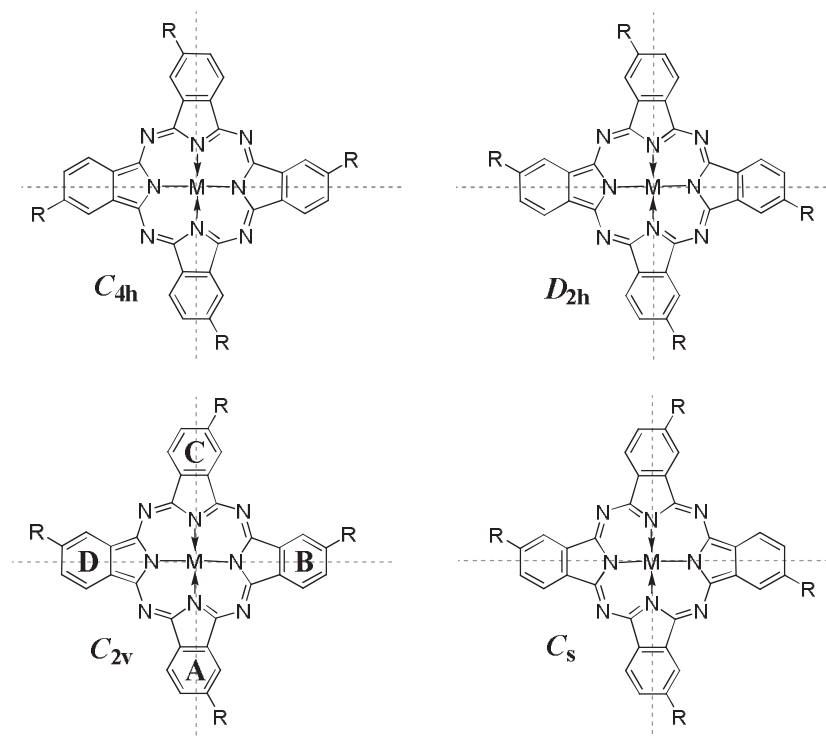
contains four signals with equal intensity of each proton of isoindole fragments with substituent R.

Synthesized phthalocyanines **2–4** were purified by a threefold column chromatography. The first column chromatography afforded one fraction containing mixture of regioisomers (for example for **4**, Figure 1). After second column chromatography also one fraction was isolated but this fraction contained the prevailing C_s regioisomer. Finally, the third column chromatography afforded one fraction containing practically pure C_s regioisomer. To the best of our knowledge, this is the very rare case, when one C_s regioisomer was separated by a simple column chromatography.

Spectral properties of the phthalocyanines received by various methods are identical. For example, UV-Vis-, IR-, ESI-mass-, ^1H NMR spectra are absolutely identical for the samples of zinc phthalocyanine **4** received from phthalonitrile **1**^[48] (symmetry was confirmed by ^1H NMR spectroscopy, see below) (path **1**→**4**), from magnesium phthalocyanine **3** (path **1**→**3**→**2**→**4**), and from metal free phthalocyanine **2** (path **1**→**2**→**4**). On the other hand, the spectra of complexes **3** and **4** practically do not differ from each other. These facts lead to the conclusion that the nature of metals (magnesium or zinc) and method of synthesis do not influence on the regioselectivity and only practically pure C_s regioisomer of complex **3** or **4** is always isolated. Considering that from phthalocyanine **3** with C_s symmetry only C_s regioisomer of phthalocyanine **2** can be synthesized, it is possible to conclude that phthalocyanine **2** obtained from phthalonitrile **1** is isolated also as C_s regioisomer.

Some bands in IR spectra of phthalocyanines **2–4** are broad because, as known,^[41] vibration bands overlap for C_s regioisomers of phthalocyanines. The $\text{C}\equiv\text{N}$ vibration bands (2230 cm^{-1} , sharp, for phthalonitrile **1**) are absent that confirm the cyclotetramerization of the phthalonitrile into the phthalocyanines (Figure 2).

The IR spectra of metal phthalocyanines **3**, **4** are practically identical and slightly differ from a spectrum of phthalocyanine ligand **2** that demonstrates small influence of the central metal on a spectral picture. For all phthalocyanines **2–4** the characteristic bands of stretching vibrations of $\text{C}_{\text{Ar}}\text{--H}$ and $\text{C}_{\text{alk}}\text{--H}$ fragments of relatively low intensity appear in the range of $3100\text{--}2800\text{ cm}^{-1}$. The low intensity band at 3291 cm^{-1} of phthalocyanine **2** is caused by stretching vibrations of N–H bonds. The intensive band of C=C bonds of aryl and hetaryl fragments of phthalonitrile **1** at 1593 cm^{-1} is shifted in high frequency area and became band of low or medium intensity at 1603 cm^{-1} for all phthalocyanines **2–4**. In the IR spectra of phthalocyanines **2–4** bands of stretching vibrations of C=C and C=N bonds of aryl and hetaryl fragments of substituents practically do not change in comparison with similar bands of phthalonitrile **1** and appear at $1511\text{--}1460\text{ cm}^{-1}$. The bands of stretching vibrations of C–N bonds of pyrazole fragments are shifted to 1393 and 1366 cm^{-1} for **4**, 1389 and 1366 cm^{-1} for **3** and 1383 and 1366 cm^{-1} for **2** and became broad in comparison with bands of phthalonitrile **1** at 1379 and 1362 cm^{-1} . In the IR spectra of phthalocyanines **2–4** new bands corresponding to the stretching vibrations of C–N bonds of pyrrole fragments in phthalocyanine core^[50] appear at 1338 and 1335 cm^{-1} for **2** and **3**, **4**, respectively. The intensive band of stretching vibrations of $\text{C}_{\text{Ar}}\text{--O--C}_{\text{Ar}}$ groups at 1251 cm^{-1} for phthalonitrile **1** is shifted to low frequency area and became broad band at 1234 , 1231 and 1232 cm^{-1} for **2**, **3**, and **4**, respectively. At the same time, the band of bending vibrations of $\text{C}_{\text{Ar}}\text{--O--C}_{\text{Ar}}$ groups at 1094 cm^{-1} for **1** is slightly shifted to 1092 , 1081 , and 1089 cm^{-1} for phthalocyanines **2**, **3**, and **4**, respectively. The bands of totally symmetric bending vibrations of isoindole fragments of phthalocyanines^[50] appear at 1113 , 1114 , and 1116 cm^{-1} for phthalocyanines **2**, **3**, and **4**, respectively. Besides,



Scheme 2. Four possible regioisomers of metal phthalocyanines with molecular symmetry C_{4h} , D_{2h} , C_{2v} and C_s

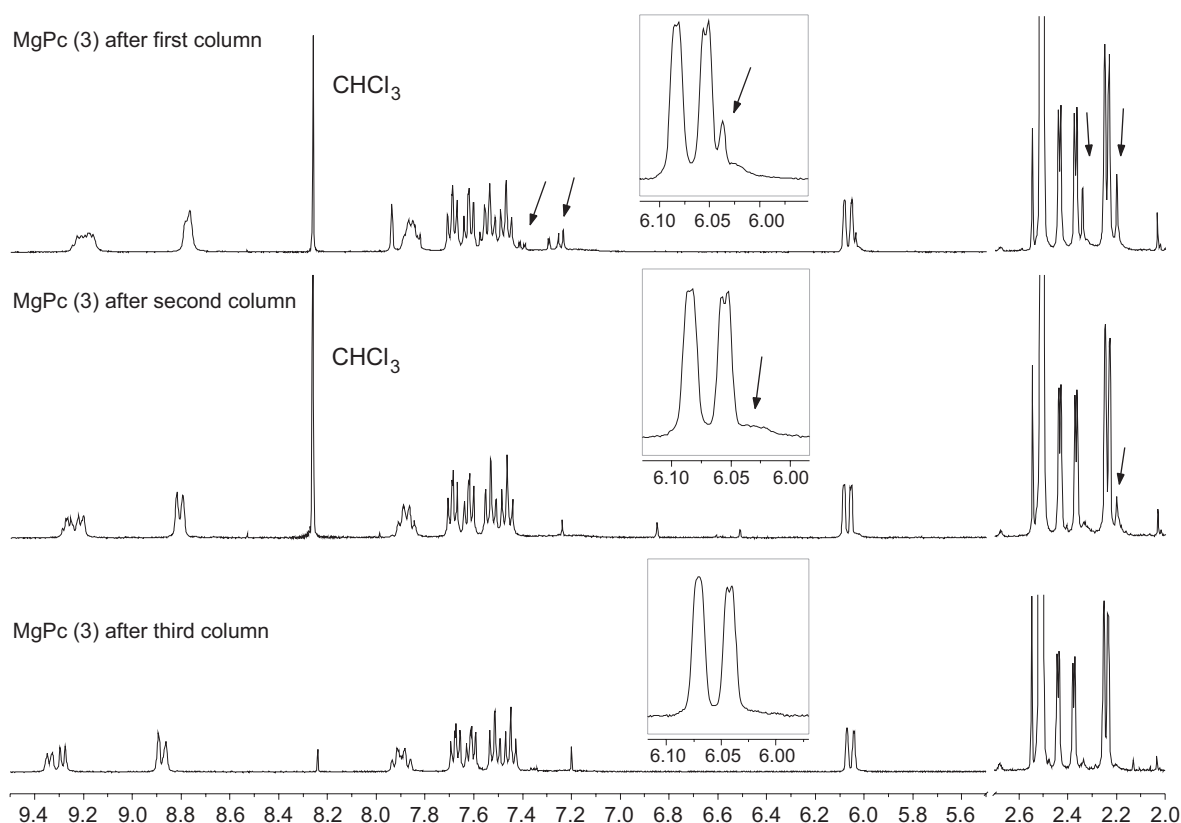


Figure 1. The evolution of ^1H NMR spectra in $\text{DMSO}-d_6$ of magnesium phthalocyanine **3** from sample containing impurity to practically pure C_s regioisomer after purification by a threefold column chromatography (the arrows show signals of protons of small amount of other isomers).

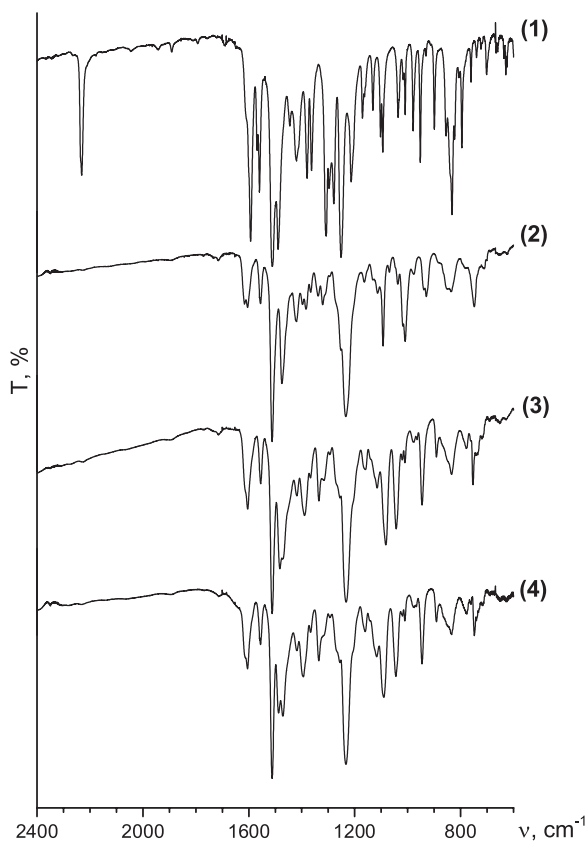


Figure 2. The IR spectra of phthalonitrile **1**, phthalocyanine **2** and its complexes with magnesium **3** and zinc **4**.

characteristic intensive bands of plane bending vibrations of $\text{C}_{\text{Ar}}-\text{H}$ bonds in phthalocyanines appear at 1037, 1044, and 1043 cm^{-1} for phthalocyanines **2**, **3**, and **4**, respectively. The low intensity band at 1009 cm^{-1} of phthalocyanine **2** is caused by bending vibrations of N–H bonds. The very characteristic bands of the out-of-plane bending vibrations of C–H bonds of aryl and hetaryl fragments appear in 900–700 cm^{-1} range. The medium band of phthalonitrile **1** at 899 cm^{-1} is shifted to low frequency area and became a broad band at 884, 890, and 891 cm^{-1} for phthalocyanines **2**, **3**, and **4**, respectively. The bands of phthalonitrile **1** at 854, 832, and 821 cm^{-1} appear as broad single bands at 834 and 833 cm^{-1} for phthalocyanines **2** and **3**, **4**, respectively. Also, bands of bending vibrations of phthalocyanine core^[50] appear at 747, 753 and 748 cm^{-1} for phthalocyanines **2**, **3**, and **4**, respectively.

It is known that high concentration of phthalocyanines cause very broad signals in ^1H NMR spectra due to aggregation.^[41–43] In order to prevent aggregation, the ^1H NMR spectra of phthalocyanines **2–4** were recorded in dilute solutions (0.5 mg per 1 mL). The ^1H NMR spectra of magnesium phthalocyanines **3** and zinc phthalocyanine **4** practically do not differ from each other. At the same time, the spectrum of metal-free phthalocyanine **2** very differs from spectra of complexes **3** and **4** (Figure 3). In the aromatic region of ^1H NMR spectrum of phthalocyanine **2** the signals of protons are observed as two unresolved multiplets integrating for 28 protons. Besides, signals of protons of pyrazole heterocycle and methyl groups are observed as broad singlets. It should be noted that this phenomenon is caused by the fact that metal-free phthalocyanine has

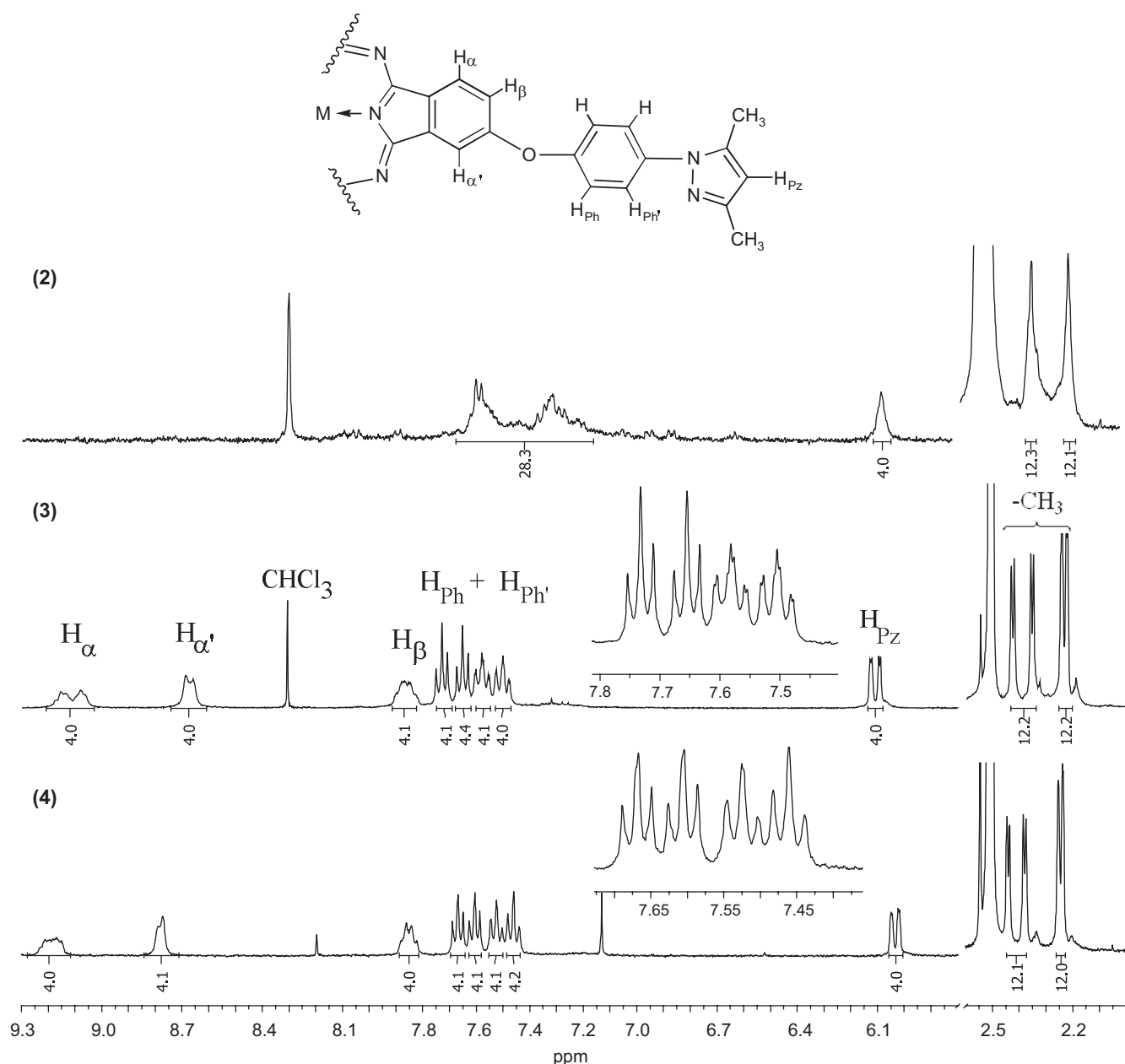


Figure 3. The ^1H NMR spectra of phthalocyanine **2** and its complexes with magnesium **3** and zinc **4**.

lower symmetry due to the absence of a four-fold axis of symmetry.^[40]

In the ^1H NMR spectra of phthalocyanines **3** and **4** the signals of protons of isoindole fragments (H_α , $\text{H}_{\alpha'}$ and H_β) appear as poorly resolved broadened multiplets in low field region. This phenomenon is caused by the fact that due to the small chemical shift difference of protons of four isoindole fragments of C_s regioisomer, a signal overlap occurs in the spectra.^[41,45] Each of the two methyl groups on the pyrazole ring gives rise to four signals in the high field region, which resembled a pair of doublets, whereas in the spectrum of phthalonitrile **1** methyl protons resonate, as might be expected as two singlets. The signals of protons in the pyrazole rings also appear by four signals like a pair of doublets, whereas in the spectrum of phthalonitrile **1** the signal of proton appears as a singlet. The signals of protons of *para*-substituted benzene rings appear by four irregular triplets against two

distorted AA'XX' doublets in the spectrum of **1**. As it follows from the ^1H – ^1H COSY data, the observed multiplicity of signals of the 3,5-dimethylpyrazole fragment is not related to spin-spin coupling (no corresponding cross peaks were detected).

It is reasonable to presume that the ^1H NMR spectral pattern is determined by nonequivalence of the four 3,5-dimethylpyrazolylphenoxy fragments, *i.e.*, the proton of each pyrazole ring resonates as a separate singlet, and the four singlets are arranged as a pair of doublets. The same is applied to the methyl protons: each peak in the pair of doublets of each methyl group is in fact a singlet of the corresponding methyl group in one of the four nonequivalent peripheral substituents. The resonance pattern observed for the *para*-substituted benzene rings may be accounted for by the AA'BB' character of aromatic system, on the one hand, and superposition of multiplets of four such systems, on

the other; as a result, four distorted triplets with complex splitting appear in the spectrum.

These phenomena confirm that the synthesized phthalocyanines **2–4** were isolated as practically pure C_s regioisomers in which all four isoindole fragments bearing peripheral pyrazolyl phenoxy groups are nonequivalent.

The ^{13}C NMR spectral data are in a good agreement with the proposed structure of phthalocyanines.

The proposed structures of phthalocyanines were also confirmed by mass spectra. The ESI mass spectra show the peaks $[\text{M}+\text{H}]^+$ and the full coincidence of experimental and calculated data that confirms the proposed structures.

The phthalocyanines **2–4** have displayed good solubility in DMF, DMSO, toluene, chloroform and acetic acid. Typical metal phthalocyanines have an unsplit lowest-energy band (Q-band) in the visible region attributed to the π - π transition from the HOMO to the LUMO of phthalocyanine ring, and B-band in the 300–500 nm region (Soret region). The electronic absorption spectra of phthalocyanine **3** and **4** show single narrow band of high intensity near 680 nm. The B-band of these phthalocyanines appears as broad band near 350 nm. The electronic absorption spectrum of metal-free phthalocyanine **2** shows splitting of Q-band at 667 and 698 nm. The Q-band practically does not depend on the substituents. For example, Q-bands for phenoxy,^[51] *tert*-butylphenoxy,^[52] (3,5-dimethyl-1*H*-pyrazol-1-yl)methoxy^[31] and (3,5-dimethyl-1*H*-pyrazol-1-yl)phenoxy^[48] substituted zinc phthalocyanines were observed at 678, 681, 680 and 682 nm respectively for solutions in DMSO. This is owing to the very small π -electronic interaction between the phthalocyanine core and aromatic substituents. Besides, central metal of phthalocyanines **3** and **4** practically does not influence on absorption spectra and Q-band appears at 680 and 678, respectively for solutions in DMF.

The phthalocyanines have a high tendency to aggregate in solutions, and mostly H-type aggregates are formed that is indicated by their broad Q-bands in the UV-Vis spectra. By aggregation, the photosensitizing ability of the Pc's is decreased by self-quenching. For generation of singlet oxygen from the phthalocyanines their aggregation behavior in different solvents therefore is an important issue.^[53]

Aggregation is usually depicted as a coplanar association of phthalocyanine rings progressing from monomer to dimer and higher order complexes. It is dependent on concentration, nature of the solvent, nature of the substituents, complexed metal ions and temperature. In this study, the aggregation behavior of the phthalocyanines **2–4** was investigated in DMF at different concentrations (Figure 4).

The aggregation behavior of the phthalocyanines **3** and **4** is practically identical. The intensity of Q-band increases with an increase of concentration of phthalocyanine **3** and **4**. The Lambert-Beer's law is obeyed in the concentration ranging from 0 to $8 \cdot 10^{-6}$ M. However, there is a deviation from the Lambert-Beer's law at higher concentration over $8 \cdot 10^{-6}$ M. The aggregation behavior of the metal-free phthalocyanine **2** is similar to aggregation behavior of the phthalocyanines **3** and **4**. However, Lambert-Beer's law is obeyed in the concentration ranging only from 0 to $5 \cdot 10^{-6}$ M. This phenomenon can be caused by the fact that DMF, being a coordinating solvent also as DMSO, binds axially to the central metal of metal phthalocyanines reducing their aggregation tendency.^[53]

Conclusions

In this paper, new phthalocyanine **2** bearing 4-(3,5-dimethyl-1*H*-pyrazol-1-yl)phenoxy groups and its complexes with magnesium **3** and zinc **4** were isolated as practically pure C_s regioisomers by column chromatography. FT-IR, ^1H NMR, ^{13}C NMR, UV-Vis and ESI mass spectroscopy data confirm the proposed structures of the synthesized phthalocyanines. It is shown that the nature of metal and reaction condition do not influence on the synthesis and isolation of practically pure C_s regioisomers. Synthesized phthalocyanines **2–4** show a good solubility in most organic solvents (*e.g.* DMF, THF, toluene, chloroform, DMSO, acetic acid). The electronic spectra of the phthalocyanines in DMF were studied at different concentrations. No aggregation was demonstrated in a range of concentrations from 0 to $8 \cdot 10^{-6}$ M for complexes and from 0 to $5 \cdot 10^{-6}$ M for metal-free phthalocyanine.

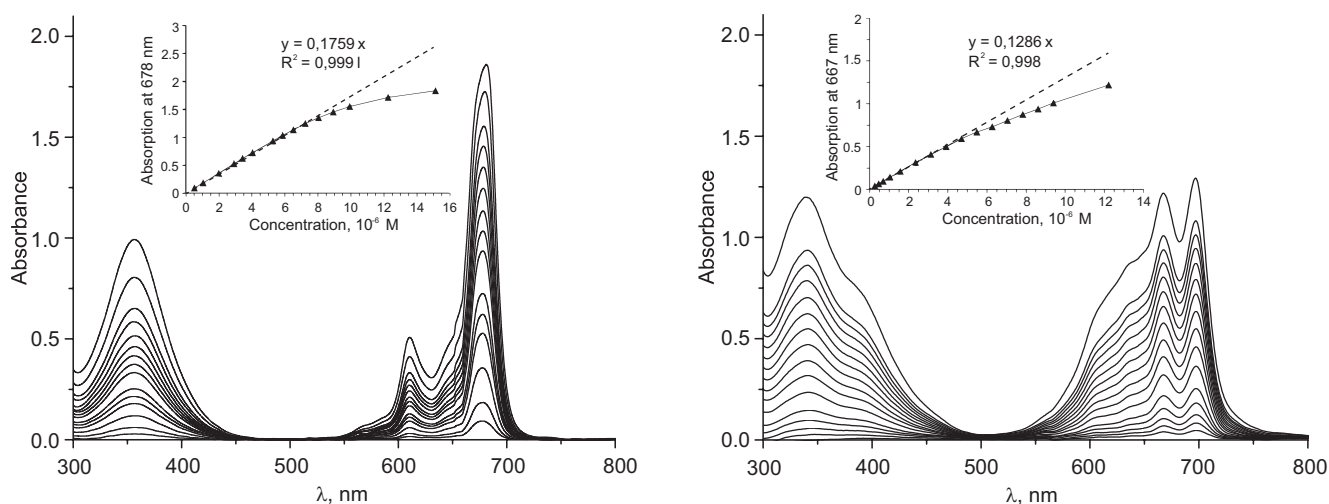


Figure 4. The absorption spectra of zinc phthalocyanine **4** (left) and metal-free phthalocyanine **2** (right) at different concentrations in DMF. Inset: Lambert-Beer law plot (dotted line – theoretical, triangle curve – experimental).

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