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New highly soluble phenoxy-substituted phthalocyanine and azaphthalocyanine derivatives: Synthesis, photochemical and photophysical studies and atypical aggregation behavior

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ABSTRACT

A series of zinc phthalocyanines and corresponding aza-analogues azaphthalocyanines substituted with peripheral 2,6-diisopropylphenoxy substituents containing different functional groups (Br, OCH_3, and OH) were synthesized and their photophysical properties were investigated. UV–vis and ^{1}H NMR analyses confirmed the non-aggregation behavior of the prepared complexes in most organic solvents. All investigated compounds showed good photophysical and photochemical properties in THF and DMF with Φ_F values in the range of 0.22–0.44 and Φ_Δ values ranging between 0.42 and 0.57. Hydroxylated compounds showed good solubility in polar solvents including ethanol, methanol, acetone and even in aqueous ethanol mixtures. Absorption spectra in aqueous ethanol indicated presence of only monomers even at very low ethanol content in water (0.5% of ethanol in water). Despite this, no fluorescence occurred from approximately 50% of ethanol in water suggesting presence of aggregates that do not differ from monomers in a shape of absorption spectra.

1. Introduction

Phthalocyanines (Pcs) and their aza-analogues (AzaPcs) from tetrapyrazinoporphyrazine group have recently received a great attention due to their fascinating optical properties which are currently being exploited in several technological applications [1–4]. Their strong absorption in the region of biological optical window (600–800 nm), efficiency in generating singlet oxygen, lack of dark toxicity, flexibility in structural modifications including the central transition metal and photostability make them promising candidates in photodynamic therapy (PDT) [5–9]. PDT is based on production of cytotoxic singlet oxygen after irradiation of photosensitizer and achieved success in clinical practice for treatment of various diseases, mainly cancer [10]. However, the aggregation behavior of Pcs represents the main concern for the researchers due to the efficiency limitation of using such material in PDT and other related applications. The aggregation leads to quenching of the excited state through nonradiative energy relaxation pathway, and as a consequence singlet oxygen production is significantly reduced [2]. Despite the fact that many approaches tried to conquer the aggregation behavior in organic solvent [11,12] or in aqueous media [13–15] there is still a room for many improvements in this area.

This work is focused on zinc Pcs and AzaPcs substituted with eight bulky phenoxy groups inhibiting the aggregation containing three different functional moieties: Br, MeO and OH. The last mentioned substitution was expected to provide Pcs and AzaPcs soluble in more polar solvents which is a good starting point for potential biological testing. Photochemical and photophysical properties of synthesized compounds were evaluated in order to gain insight to the structure-property relationships. Based on previous findings, zinc complexes have been chosen in this study as a result of their desirable photophysical and stability properties.

2. Experimental

2.1. Material and method

The 4,5-dichlorophthalonitrile and precursor 5,6-dichloropyrazine-2,3-dicarbonitrile were synthesized by the reported procedures in the literature [16,17]. Starting from the 2,6-di-*iso*-

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propylphenol, 2,6-di-*iso*-propyl-4-bromophenol and 2,6-di-*iso*-propyl-4-methoxyphenol were synthesized and characterized in our laboratory [18]. 4,5-Bis(2,6-di-*iso*-propyl-4-bromophenoxy)phthalonitrile (**1**) and 2,3,9,10,16,17,23,24-octa(2,6-di-*iso*-propyl-4-bromophenoxy)phthalocyaninato zinc (II) (**5**) have been reported previously by our group [19]. Anhydrous DMF was purchased from Aldrich and the potassium carbonate was obtained locally. ^{1}H NMR spectra (400 MHz) were recorded using Bruker DPX 400. IR spectra were recorded on a Jasco 6300 FTIR. UV–Vis studies were done on a Varian Cary 5 spectrometer and Shimadzu UV-2401Pc spectrophotometer. Elemental analyses were carried out using Elementar Vario Micro Cube. Mass analyses were done by electron impact (EI) and fast atom bombardment (FAB) on a Thermo DFS mass spectrometer. Differential scanning calorimetry (DSC) analyses were carried out on Shimadzu DSC-50. Fluorescence spectra were obtained using an AMINCO-Bowman series 2 luminescence spectrometer (SLM-Amino, Urbana II, U.S.A).

2.2. Synthesis

2.2.1. 4,5-Bis(2,6-diisopropyl-4-methoxyphenoxy)phthalonitrile (**2**)

To the stirred solution of 2,6-di-*iso*-propyl-4-methoxyphenol (4.64 g, 22.3 mmol) in dry DMF (50 mL) finely grounded anhydrous CsF (6.78 g, 44.6 mmol) followed by 4,5-dichlorophthalonitrile (2 g, 10.1 mmol) were added. The reaction mixture was heated at 60 °C under nitrogen atmosphere for 24 h. After cooling the reaction mixture was poured into distilled water. The precipitate was filtered and washed with distilled water. The crude product was then recrystallised from methanol to give **2** as white crystalline solid (4.1 g, 75%), M.p: 192 °C; IR (KBr) ν/cm^{-1}: 2226 (CN). ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 6.81 (s, 4H, ArH), 6.8 (s, 2H, ArH), 3.90 (s, 6H, CH_3O), 2.78 (sept, 4H, $J = 6.8$ Hz, CH), 1.24 (d, 12H, $J = 6.8$ Hz, CH_3), 1.16 (d, 12H, $J = 6.8$ Hz, CH_3). Anal. calc. for $C_{34}H_{40}N_2O_4$, C: 75.53, H: 7.46, N: 5.18. Found C: 75.45, H: 7.84, N: 5.08; MS (EI) (*m/z*): Calc. 540.3. Found 540 [M]$^+$.

2.2.2. 5,6-Bis(4-bromo-2,6-diisopropylphenoxy)pyrazine-2,3-dicarbonitrile (**3**)

Dry potassium carbonate (8.3 g, 60.0 mmol) was added to a solution of 2,6-di-*iso*-propyl-4-bromophenol (11.35 g, 45.0 mmol) and 5,6-dichloropyrazine-2,3-dicarbonitrile (2.9 g, 15.0 mmol) in dry DMF (150 mL). The reaction mixture was heated at 60 °C for 24 h under nitrogen. On cooling, the reaction mixture was poured in to distilled water (200 mL). The resulting precipitate was collected by filtration and washed with water and air-dried. The crude product was recrystallised from methanol to give **3** as a white powder (7.8 g, 82%); M.p: 203–204 °C; IR (KBr) ν/cm^{-1}: 2238 (CN); ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.40 (s, 4H, ArH), 2.76 (sept, 4H, $J = 6.8$ Hz, CH), 1.23 (d, 24H, $J = 6.4$ Hz, CH3), Anal. calc. for $C_{30}H_{32}N_4O_2Br_2$, C: 56.33, H: 5.00, N: 8.76, Found C: 56.06, H: 4.91, N: 8.62; MS (EI) (*m/z*): Calc. 639.8, Found 640[M]$^+$.

2.2.3. 5,6-Bis(2,6-diisopropyl-4-methoxyphenoxy)pyrazine-2,3-dicarbonitrile (**4**)

To the stirred solution of 2,6-di-*iso*-propyl-4-methoxyphenol (4.59 g, 22 mmol) in dry DMF (50 mL) finely grounded anhydrous CsF (6.71 g) followed by 5,6-dichloropyrazine-2,3-dicarbonitrile (2 g, 10 mmol) was added. The reaction mixture was heated at 60 °C under nitrogen atmosphere for 24 h. After cooling the reaction mixture was poured in to distilled water. The precipitate was filtered and washed with distilled water. The crude product was then recrystallised from methanol to give **4** as white crystalline solid (4.35 g, 80%); M.p: 190 °C; IR (KBr) ν/cm^{-1}: 2226 (CN). ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 6.76 (s, 4H, ArH), 3.87 (s, 6H, CH_3O), 2.78 (sept, 4H, $J = 6.8$ Hz, CH), 1.21 (d, 24H, $J = 6.1$ Hz, CH3); Anal. calc. for $C_{32}H_{38}N_4O_4$, C: 70.82, H: 7.06, N: 10.32. Found C: 71.08, H: 7.3, N: 10.00; MS (EI) (*m/z*): Calc. 542.289, Found 542 [M]$^+$.

2.2.4. 2,3,9,10,16,17,23,24-octa(2,6-diisopropyl-4-methoxyphenoxy)phthalocyaninato zinc(II) (**6**)

Compound **1** (0.50 g, 0.92 mmol) was reacted with excess of anhydrous zinc acetate (40 mg, 0.22 mmol) in dry quinoline (10 mL) at 180 °C under nitrogen for 8 h. The crude product was purified by column chromatography on SiO_2 eluting with hexane/DCM/ethyl acetate (7:2:1) to give **6** as a green solid. (0.36 g, 70%), M.p over 300 °C; UV/vis ($CHCl_3$): λ_{max} 683 (5.56), 356 nm; IR (KBr) ν/cm^{-1}:2963, 1606, 1453, 1398, 1336, 1303, 1266, 1185, 1125, 1090, 1039, 888, 846; ^{1}H NMR (400 MHz; $CDCl_3$) δ/ppm: 8.28 (s, 8H, ArH), 6.97 (s, 16H, ArH), 4.08 (s, 24H, CH_3O), 3.45 (sept, 16H, $J = 6.8$ Hz, CH), 1.27 (br, 96H, CH_3); Anal. calc. for $C_{136}H_{164}N_8O_{18}$ Zn (compound **6** + $2H_2O$): C 72.4, H 7.30, N 4.95, found C 72.32, H 7.80, N 4.84; MS (FAB) (*m/z*): Calc. 2225, Found: 2226 [M + H]$^+$.

2.2.5. 2,3,9,10,16,17,23,24-cta-(2,6-diisopropyl-4-hydroxyphenoxy) phthalocyaninato zinc(II) (**7**)

To a solution of compound **5** (0.200 g, 0.1 mmol) in dry DCM (10 mL), under nitrogen, at 0 °C boron tribromide (0.1 mL, 2 mmol) was added dropwise. After 6 h the stirring was stopped and the solution was transferred to a beaker; excess of boron tribromide was left to evaporate 24 h at room temperature then the reaction was quenched with distilled water and a purple precipitate crushed out. The solid was collected, dissolved in ethyl acetate and washed with water. The organic layer was dried over magnesium sulphate and evaporated to give **7** as a green solid that was purified by recrystallization using ethyl acetate/hexane (0.095 g, 56%), M.p over 300 °C; UV/vis (EtOH): λ_{max} 677 (5.60), 356 nm; IR (KBr) ν/cm^{-1} 3406, 2963, 1603, 1482, 1445, 1397, 1338, 1306, 1264, 1220, 1184, 1141, 1089, 1025, 888, 853; ^{1}H NMR (400 MHz; acetone[D_6]) δ/ppm: 8.84 (s br, 8OH), 8.28 (s, 8H, ArH), 7.13 (s, 16H, ArH), 3.45 (sept, 16H, $J = 6.5$ Hz, CH), 1.22 (d br, 96H, CH_3); Anal. calc. for $C_{128}H_{148}N_8O_{18}Zn$ (compound **7** + $2H_2O$): C 71.44, H 6.93, N 5.21, found C 71.80, H 7.34, N 5.03; MS (FAB)(*m/z*): Calc. 2113, Found: 2113 [M]$^+$.

2.2.6. 2,3,9,10,16,17,23,24-octa(4-bromo-2,6-diisopropylphenoxy)-1,4,8,11,15,22,25-octaazaphthalocyaninato zinc(II) (**8**)

A mixture of 5,6- Bis(2,6-di-*iso*-propyl-4-bromophenoxy)pyrazine-2,3-dicarbonitrile (**3**) (1.00 g, 1.6 mmol) and an excess of anhydrous zinc (II)acetate (40 mg, 0.22 mmol) in dry quinoline (10 mL) was stirred at 180 °C under nitrogen atmosphere for 6 h. The reaction mixture was poured into stirred methanol (20 mL) on cooling, and the solid green product was collected by filtration then washed intensely with warm water and methanol. The crude product was purified by column chromatography on silica gel where $CHCl_3$ was used as the eluting solvent. Following the removal of the solvent by evaporation to give **8** as a green solid (0.40 g, 39%); M.p over 300 °C; UV/vis (DMF): λ_{max} 636 (5.39), 365 nm; IR (KBr) ν/cm^{-1}: 3390, 2969, 2931, 1576, 1550, 1451, 1420, 1400, 1362, 1213, 1160, 952, 932; ^{1}H NMR (400 MHz; $CDCl_3$) δ/ppm: 7.70 (s, 16H, ArH), 3.37 (sept, 16H, $J = 6.8$ Hz, CH), 1.34 (br, 96H, CH_3); Anal. calc. for $C_{120}H_{128}$ $Br_8N_{16}O_8Zn$: C, 54.86; H, 4.88; N, 8.53. Found: C, 55.1; H, 5.20; N, 8.90. MS (FAB) *m/z*: Calc. 2625, Found: 2625 [M]$^+$.

2.2.7. 2,3,9,10,16,17,23,24-octa(2,6-diisopropyl-4-methoxyphenoxy)-1,4,8,11,15,22,25-octaazaphthalocyaninato zinc(II) (**9**)

5,6-Bis(2,6-di-*iso*-propyl-4-methoxyphenoxy)pyrazine-2,3-dicarbonitrile (0.500 g, 0.9 mmol) was reacted with anhydrous zinc acetate (0.1 g, 0.55 mmol) in quinoline (10 mL) at 180 °C under nitrogen atmosphere for 6 h. The crude product was purified by column chromatography on SiO_2 eluting with hexane/DCM (4:6) to give **9** as a green solid (0.360 g, 70%); M.p over 300 °C; UV/vis ($CHCl_3$): λ_{max} 629 (5.44), 360 nm; IR (KBr) ν/cm^{-1} 2970, 1599, 1463, 1402, 1300, 1197, 1161, 1128, 951, 817; ^1H NMR (400 MHz; $CDCl_3$) δ/ppm: 6.97 (s, 16H, ArH), 4.08 (s, 24H, CH_3O), 3.33 (sept, 16H, $J = 6.8$ Hz, CH), 1.28 (d, 96H, $J = 7.21$ Hz, CH_3); Anal. calc. for $C_{128}H_{154}N_{16}O_{17}Zn$ (compound **9** + H_2O): C 68.20, H 6.89, N 9.94, found C 68.26, H 6.87, N 9.75; MS (FAB) (*m/z*): Calc. 2233, Found:2233 [M]$^+$.

*2.2.8. 2,3,9,10,16,17,23,24-octa(4-hydroxy-2,6-diisopropylphenoxy)-1,4,8,11,15,22,25-octaazaphthalocyaninato zinc(II) (**10**)*

Complex **10** was synthesized and purified using the similar procedure adopted for **7** (0.120 g, 60%); M.p over 300 °C; UV/vis (EtOH): λ_{max} 625(5.35), 360 nm; IR (KBr) ν/cm^{-1} 3406, 2963, 1603, 1482, 1445, 1397, 1338, 1264, 1184, 1089, 1025, 888, 853; ^1H NMR (400 MHz; acetone[D_6]) δ/ppm: 8.66 (br s, 8OH), 7.06 (s, 16H, ArH), 3.34 (sept, 16H, $J = 6.5$ Hz, CH), 1.30 (br, 96H, CH_3); Anal. Calc. for $C_{120}H_{140}N_{16}O_{18}Zn$ (compound **10** + $2H_2O$): C 66.73, H 6.53, N 10.38, found C 66.55, H 6.84, N 9.97; MS (FAB) (*m/z*): Calc. 2121, Found: 2121 [M]$^+$.

2.3. Photophysical and photochemical parameters

2.3.1. Fluorescence quantum yields

Fluorescence quantum yields (Φ_F) of the studied Pcs and AzaPcs were determined in THF and DMF and calculated by using the following equation (Eq. (1)) [20]:

$$\Phi_F^S = \Phi_F^R \left(\frac{F^S}{F^R}\right) \left(\frac{1 - 10^{-A^R}}{1 - 10^{-A^S}}\right) \left(\frac{n^S}{n^R}\right)^2 \qquad (1)$$

Where Φ_F is the fluorescence quantum yield, *F* is the area under the fluorescence emission curve, *A* is the absorbance at the excitation wavelength and *n* is the refractive index of the solvent. Superscripts *R* and *S* indicate reference and sample, respectively. Unsubstituted zinc (II) phthalocyanine (ZnPc) was used as the reference ($\Phi_{F(chloronaphthalene)} = 0.30$ [21]). Both reference and sample were excited at the same wavelength ($\lambda_{exc} = 591$ nm for AzaPcs, $\lambda_{exc} = 611$ nm for Pcs). In order to avoid inner filter effect, absorbance at Q-band maximum was kept below 0.05. All experiments were performed three times and the data presented in the paper represent a mean of these three experiments. Estimated error ±10%. Excitation spectra were collected by observing fluorescence signal usually at 700 nm or 740 nm for AzaPc and Pc, respectively.

2.3.2. Singlet oxygen quantum yields

The measurements of singlet oxygen quantum yields (Φ_Δ) were performed in DMF and THF based on decomposition of a chemical trap 1,3-diphenylisobenzofuran (DPBF) [22]. ZnPc was used as a reference compound ($\Phi_{\Delta(DMF)} = 0.56$ [23,24], $\Phi_{\Delta(THF)} = 0.53$ [25]). In detail the procedure was as follows: 2.5 mL of a stock solution of DPBF (5×10^{-5} M) in DMF or THF was transferred into a 10 × 10 mm quartz optical cell and bubbled with oxygen for 1 min. Defined amount (usually 30 µl) of concentrated stock solution of the tested compound in DMF or THF was then added. Absorbance of the final solution in Q-band maximum was always about 0.1. The solution was stirred and irradiated for defined times using a halogen lamp (Tip, 300 W). Incident light was filtered through a water filter (6 cm) and an orange HOYA G filter to remove heat and light under 506 nm, respectively. Decrease of DPBF concentration in DMF or THF solution with irradiation time was monitored at 415 nm or 414 nm, respectively. No significant changes in Q-band shape or intensity were observed indicating that the Pcs and AzaPcs were not decomposing or aggregating within the experimental period. All experiments were performed three times and the data presented in the paper represent a mean of these three experiments. Estimated error ±10%. Singlet oxygen quantum yield (Φ_Δ) was calculated by using the following equation (Eq. (2)):

$$\Phi_\Delta^S = \Phi_\Delta^R \frac{k^S I_{aT}^R}{k^R I_{aT}^S} \qquad (2)$$

where *k* is a slope of a plot of the dependence of ln (A_0/A_t) on irradiation time *t*, with A_0 and A_t being the absorbance of the DPBF at monitoring wavelength before irradiation and after irradiation time *t*, respectively. I_{aT} is a total amount of light absorbed by the dye. Superscripts *R* and *S* indicate reference and sample, respectively. I_{aT} is calculated as a sum of intensities of the absorbed light I_a at wavelengths from 506 nm to 800 nm (step 0.5 nm). Light under 506 nm is completely filtered off by HOYA G filter and light above 800 nm is not absorbed by the dyes. I_a at given wavelength is calculated using Beer's law (Eq. (3)).

$$I_a = I_0\left(1 - e^{-2.3A}\right) \qquad (3)$$

Where transmittance of the filter at given wavelength stays for I_0 and absorbance of the dye at this wavelength stays for *A*.

2.4. Study of aggregation properties

Absolute ethanol (99%, Sigma–Aldrich) was used to prepare 200 µM stock solutions of **7** and **10**. The stock solution was diluted 200 × with premixed ethanol/water mixtures (from pure ethanol to pure water) to obtain final 1.0 µM solution that was used for absorbance measurements. For fluorescence measurements, the solutions were further diluted to obtain maximum absorbance of 0.05 in Q-band (for excitation wavelengths and calculations see above). Refractive indices were measured for each ethanol/water ratio (see Supporting Information) and used to correct Φ_F values according to Eq. (1).

3. Result and discussion

3.1. Synthesis and characterization

Fig. 1 shows the synthetic route for the target Pc (**5**–**7**) and AzaPc (**8**–**10**) derivatives. The starting phthalonitrile (**1**, **2**) and pyrazine-2,3-dicarbonitrile (**3**, **4**) precursors were prepared in a good yield from the aromatic nucleophilic substitution reaction between 4,5-dichlorophthalonitrile or 5,6-dichloropyrazine-2,3-dicarbonitrile respectively with the appropriately functionalized phenolate. The synthesis of zinc complexes (**5**, **6**, **8** and **9**) was achieved by metal-ion mediated cyclotetramerisation reaction of the corresponding precursors (**1**–**4**) in dry quinoline using anhydrous zinc acetate. Subsequent demethylation of Pc **6** and AzaPc **9** using an excess of BBr_3 in DCM gave Pc **7** and AzaPc **10**, respectively. The routine characterization techniques such as UV–vis, IR, elemental analysis and fast atom bombardment mass spectroscopy (FAB MS) gave results consistent with the proposed structures for all the prepared complexes along with their satisfactory purities. Pcs and AzaPcs exhibited well-resolved ^1H NMR spectra with sharp peaks in both aromatic and aliphatic region implying that the aggregation behavior is absent (see Supporting Information). The NMR spectra of starting precursors and their corresponding complexes were almost identical and showed exactly the same excellent quality spectra apart from the chemical shifts resulting from the ring current effect of the aromatic macrocycle which caused the deshielding effects [26]. This is

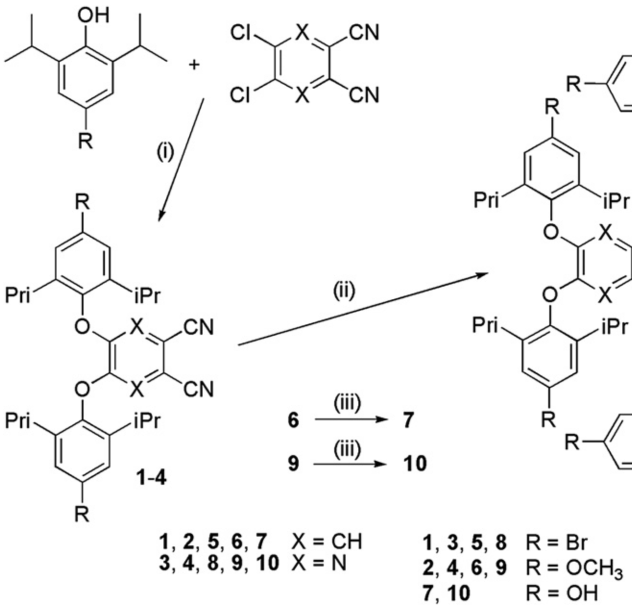

Fig. 1. The synthesis of ZnPcs and ZnAzaPcs. Reagents and conditions: i) CsF or K_2CO_3, DMF, 60 °C, 24 h, ii) zinc acetate, quinoline, 180 °C, 6–8 h, iii) BBr_3/DCM 0–5 °C, 6 h.

consistent with the previous reports which showed that the isolated forms of complexes in either dilute or concentrated solution appeared to be intrinsically related to the conformation adapted by the eight peripheral bulky groups which efficiently suppressed the cofacial interactions between the macrocycle cores as revealed by both UV–Vis (see below) and ^{1}H NMR spectroscopic techniques [11,26]. The synthesized compounds showed characteristic absorption spectra with B-bands located in area around 360 nm and a Q-bands located over 630 nm. The B-band was found more intense for all AzaPcs when compared to corresponding Pcs (Fig. 2). Interestingly, the Q-bands of all AzaPcs were strongly blue-shifted by approximately 50 nm when compared with corresponding Pcs (Fig. 2). This observation has already been made previously [27], and recently explained by molecular calculations to be due to stronger destabilization of LUMO than HOMO by pyrazine rings in AzaPcs when compared to benzene rings in Pcs [28].

3.2. Photophysical and photochemical properties

Photophysical and photochemical properties of all studied Pcs and AzaPcs were determined in DMF and THF. All compounds showed strong fluorescence signal after excitation with a shape of the fluorescence emission spectra characteristic for similar compounds (Fig. 3). The Stokes shifts were very small (Table 1). Interestingly, the Stokes shift around 4–5 nm was observed for Pcs, but almost doubled for AzaPcs (approximately 7–9 nm). As mentioned above, all compounds were present in the monomeric form which was further confirmed by comparison of the fluorescence excitation spectra with the absorption spectra. Both spectra superposed (Fig. 3) indicating that only monomeric form is present in solution. The aggregates have different absorption spectra than monomers but they usually do not fluoresce besides few exceptions of J-dimers [29,30]. For this reason, a perfect accordance of excitation and absorption spectra may serve as a confirmation of fully monomeric form. Fluorescence quantum yields (Φ_F) were of typical range for zinc complexes of Pc and AzaPc [31]. An observation was made from the data presented in Table 1, that the Φ_F values of

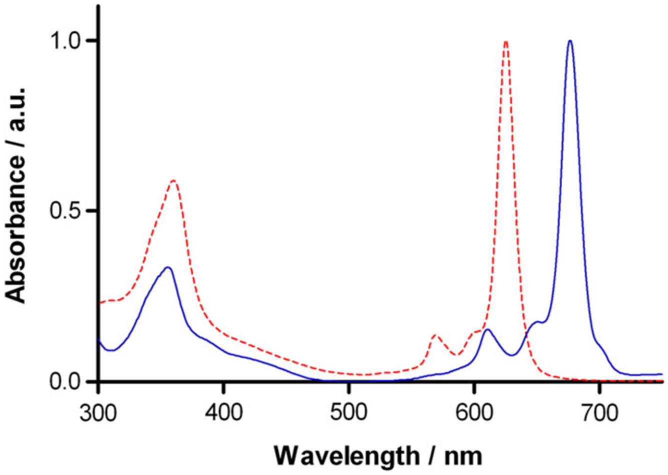

Fig. 2. Absorption spectra of compounds **7** (full line) and **10** (dashed line) in ethanol. Spectra were normalized to the same absorption in Q-band.

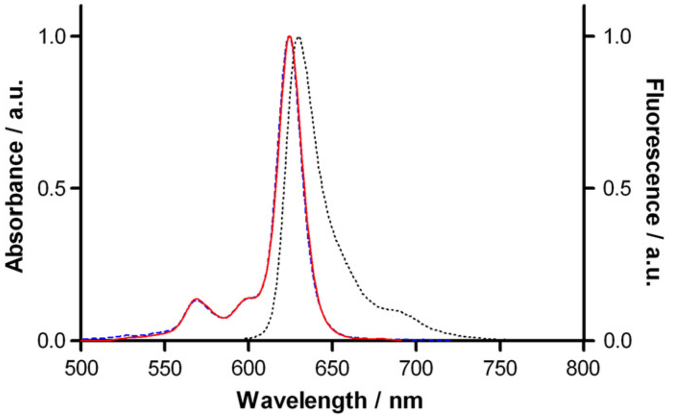

Fig. 3. Normalized absorption (dashed), emission (dotted) and excitation (full, overlaps with absorption spectrum) of compound **10** in THF.

Table 1
Photochemical and photophysical properties of studied compounds in DMF and THF.[a]

Complex	Substituent	Core	Φ_F[b]	Φ_Δ[b]	Q-band λ_{max} (nm)	λ_{em} (nm)	Stokes shift (nm)
5	Br	Pc	0.25/0.27	0.59/0.57	676/676	681/680	5/4
6	OCH_3	Pc	0.21/0.23	0.59/0.57	679/678	683/682	4/4
7	OH	Pc	0.23/0.27	0.54/0.50	678/677	683/681	5/4
8	Br	AzaPc	0.30/0.39	0.57/0.53	629/627	638/634	9/7
9	OCH_3	AzaPc	0.28/0.34	0.55/0.51	629/626	637/633	8/7
10	OH	AzaPc	0.22/0.44	0.42/0.50	628/624	636/630	8/6

Estimated error 10%.
[a] Presented as value in DMF/value in THF.
[b] Mean of three independent experiments.

AzaPcs were always higher than those of Pcs and that the values for the same compound in THF exceeded those in DMF.

Singlet oxygen quantum yields (Φ_Δ) were determined using decomposition of its chemical scavenger 1,3-diphenylisobenzofuran (DPBF). Singlet oxygen is considered as the main phototoxic species in PDT and that is why a rate of its production belongs among the important parameters of all new photosensitizers [32]. The Φ_Δ of all compounds in this work exceeded the value of 0.50 indicating very good singlet oxygen production that is fully satisfactory for potential application in PDT. Focusing on the data in Table 1, reverse conclusions than those raised for Φ_F could be made. Pcs were shown to be stronger singlet oxygen producers than AzaPcs and higher Φ_Δ values were usually obtained in DMF than in THF. A simple conclusion can be made that Pc core supports energy dissipation from excited state through singlet oxygen more than AzaPc with the same substitution pattern. On the other hand, AzaPc core seems to be a stronger fluorophore, an important fact which may lead to development of fluorescent probes in future. The results are in good agreement with a previously published data where Pcs and AzaPcs with the same peripheral substituents were compared [33]. Focusing on the nature of peripheral substitution, an increase of Φ_Δ on the account of Φ_F could be expected for compounds **5** and **8** substituted with bromine due to heavy atom effect. This well-known phenomenon was demonstrated on several examples showing that substitution by heavy atoms changes excited states deactivation pathways by preferring intersystem crossing over fluorescence [34,35]. However, no significant increase of singlet oxygen production or decrease of fluorescence was observed for compounds **5** and **8**. Changes in electron density transmitted inductively from bromo substituent to macrocycle are apparently too weak to induce any difference in photophysical and photochemical properties.

3.3. *Aggregation behavior*

The assessment of aggregation behavior for the prepared complexes (**5**, **6**, **8** and **9**) was done by recording the absorption spectra in different organic solvents (CH_2Cl_2, $CHCl_3$, THF and DMF) (Supporting Information). The single unperturbed Q-band peak, a typical of non-aggregated species, was the characteristic feature of each complex spectrum. Interestingly, the hydroxylated derivatives (**7** and **10**) were highly soluble in methanol, ethanol and acetone and showed no evidence of self association as shown by the position and the appearance of the intense Q-band as well as strong fluorescence. For example, the absorption spectra of complexes **7** and **10** showed a monomeric character (i.e. single sharp Q-band at λ_{max} 677 and 625 nm, respectively) even at concentration of 100 μM. The shape of the spectra remained constant and their molar extinction coefficients obeyed the Beer–Lambert law in wide range of concentration from 0.25 μM to 100 μM (Fig. 4 and Supporting Information).

Interestingly, ethanol solutions of compounds **7** and **10** can be mixed with water in various ratios and the compounds remain still fully dissolved (tested up to 0.5% of ethanol in water). Surprisingly, the shape of the Q-band remained mostly unchanged and the absorption spectrum indicated presence of only monomeric form (Fig. 5 and Supporting Information). However, when the solutions containing more than 50% of water were exposed to UV light (366 nm) no fluorescence occurred (Supporting Information). For this reason, a careful analysis of behavior of these compounds in

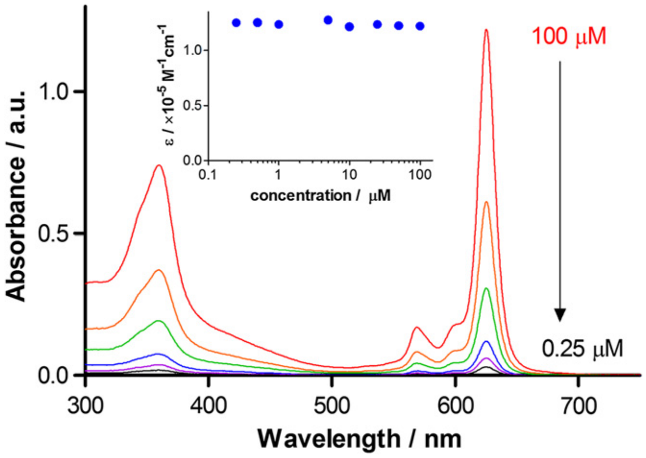

Fig. 4. Absorption spectra of compound **10** in ethanol at different concentrations ranging from 100 μM to 0.25 μM. Spectra from 100 μM to 10 μM were measured in cuvettes with 1 mm optical pathlength. Inset: Dependence of extinction coefficient in Q-band on concentration.

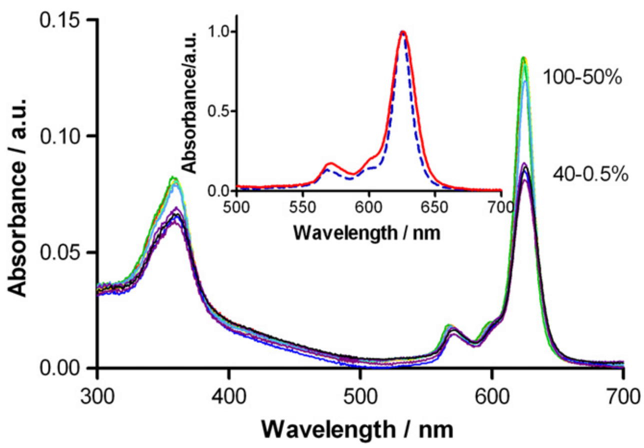

Fig. 5. Absorption spectra of compound **10** in ethanol/water mixtures. Numbers represent content of ethanol in water. Concentration of the sample was kept at 1.0 μM in all cases. Inset: Normalized spectra of compound **10** in ethanol (dashed) and water containing 10% of ethanol (full).

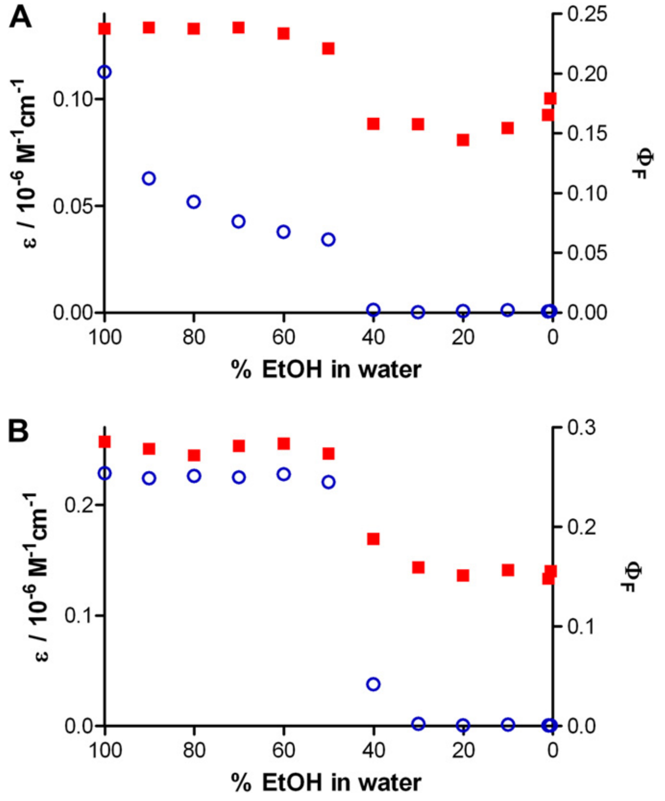

Fig. 6. Dependence of extinction coefficient (full squares) and fluorescence quantum yield (open circles) of compound **10** (A) and **7** (B) on content of ethanol in water. Extinction coefficients were measured at concentration of 1.0 uM for all data. Excitation wavelengths for fluorescence quantum yield determination were 591 nm and 611 nm for **10** and **7**, respectively.

solutions containing different ethanol/water ratios was performed. As obvious from Fig. 5, the absorption spectra remained unchanged from absolute ethanol up to approximately 50% of ethanol in water (concentration of the dyes was kept constant at 1.0 μM for all tested ratios). At this ratio, a significant drop in extinction coefficient for more than one third of the value was observed (Fig. 6). Lower content of ethanol in water did not lead to further changes and the extinction coefficient remained constant up to the lowest ratio tested. Interestingly, the shape of the spectrum did not change, the only difference was a very small broadening and a red-shift of the Q-band of compound **7**. The measurements of fluorescence properties complemented the absorption spectra analysis. Fluorescence quantum yields of both compounds in absolute ethanol reached values 0.25 and 0.20 for **7** and **10**, respectively, which is fully comparable with the values obtained in DMF (see Table 1). The Φ_F values of **7** remained high up to 50% of ethanol in water and then a drastic drop to almost zero values was observed at lower content of ethanol. The changes followed the changes of extinction coefficient. Similar drop of the Φ_F values was detected also for compound **10** from 50% of ethanol but in this case the decrease of the values started already after adding small amount of water. In general, decrease or complete disappearance of fluoresce signal indicates strong aggregation which is most likely also the case of compounds **7** and **10**. The aggregation of Pc or AzaPc macrocycles is usually accompanied by significant changes in absorption spectra in the Q-band. Surprisingly, this was not the case of these compounds and the spectra at lower content of ethanol in water can be easily misinterpreted (Fig. 5, inset). At this moment, the most likely explanation is that Pc **7** and AzaPc **10** form atypical type of aggregate with no fluorescence but almost no changes in absorption spectra. This behavior may be closely connected with extremely bulky peripheral substituents precluding close approximation of two molecules.

4. Conclusion

Zinc phthalocyanines and their heteroatomic analogues azaphthalocyanines peripherally substituted with bulky phenoxy moieties containing different functional groups were prepared and their photophysical and photochemical properties have been investigated. The fluorescence and singlet oxygen quantum yields of the studied complexes gave good indication of their potential as photosensitizer in PDT applications. All complexes showed truly non-aggregating behavior in most organic solvents. Interestingly, the hydroxylated derivatives (**7** and **10**) exhibited unusual aggregation properties in ethanol/water mixtures at lower than 50% content of ethanol. Fluorescence measurements of the last mentioned compounds indicated strong aggregation but the absorption spectra retained character typical for monomeric species besides slightly lower extinction coefficient. These results pointed out the importance of fluorescence determination during assessment of aggregation behavior since the absorption measurements could easily lead to incorrect interpretation.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.dyepig.2012.03.023.

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