



Synthesis, photophysical and photochemical properties of quinoline substituted zinc (II) phthalocyanines and their quaternized derivatives

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ABSTRACT

The new tetrakis-(6-oxyquinoline)phthalocyaninato zinc (II) (**5**), octakis-(6-oxyquinoline)phthalocyaninato zinc (II) (**6**) and their quaternized derivatives (**5a** and **6a**) have been synthesized and characterized. Photophysical and photochemical properties of 6-oxyquinoline appended zinc (II) phthalocyanines are investigated in dimethylsulfoxide (DMSO) for both the non-ionic (**5** and **6**) and quaternized ionic (**5a** and **6a**) complexes and in phosphate buffered solution (PBS) for quaternized ionic complexes. General trends are described for photodegradation quantum yields, fluorescence quantum yields and fluorescence lifetimes as well as singlet oxygen quantum yields of these compounds. In this study, the effects of the position and number of the substituents, and quaternization of the substituents on the photophysical and photochemical parameters of the zinc (II) phthalocyanines are also reported. A spectroscopic investigation of the binding of the quaternized ionic zinc (II) phthalocyanine complexes to bovine serum albumin (BSA) is also presented in this work.

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1. Introduction

Phthalocyanines (Pcs), a family of aromatic macrocycles based on an extensive delocalized 18 π electron system, have been extensively studied due to their unique optical, electronic, catalytic and structural properties. Particularly, they have been studied as dyes and pigments, light emitting diodes, in optical limiting devices, in molecular electronics, for non-linear optical applications, as liquid crystals, gas sensors, semiconductor materials, in photovoltaic cells, photodynamic therapy (PDT) of cancer and for electrochromic displays [1–3].

PDT is an effective single modality treatment for several medical indications, including cancer, age-related maculopathy, periodontitis, malignant and pre-malignant skin disorders [4–6]. PDT involves the uptake of the photosensitizing compound (photosensitizer) by cancerous tissues or other sites of therapeutic interest (e.g. neovascular regions), followed by selective irradiation with visible or IR light of an appropriate wavelength that is absorbed by the photosensitizer [7–9]. Three fundamental requirements for PDT are oxygen, light source, and photosensitizer. Each factor is harmless by itself, but their combination can produce cytotoxic agents. In PDT, the photosensitizer preferentially localizes in rapidly growing cells and gets activated by the exposure of light in presence of

oxygen to generate reactive oxidative species (ROS) such as singlet oxygen as well as other ROS to kill tumor cells [10].

The first photosensitizers are hematoporphyrin derivatives and have already been described in detail in several articles [11,12]. Second generation photosensitizers such as phthalocyanines have also been introduced for PDT in research and clinical trials [13]. Several phthalocyanine systems such as the silicon (IV) phthalocyanine Pc4 and a liposomal preparation of zinc (II) phthalocyanine have been in clinical trials. Photosens[®], which is a mixture of sulfonated aluminium (III) phthalocyanines, is clinically used in Russia for the treatment of a range of cancers [14]. Due to their high molar absorption coefficient in the red part of the spectrum, photostability and long lifetimes of the photoexcited triplet states, Pcs are known to be useful photosensitizers [15–18]. Especially, ZnPcs have been extensively studied since the d^{10} configuration of the central Zn^{2+} ion results in optical spectra that are not complicated by additional bands, as in transition-metal complexes. ZnPcs have intensive red-visible region absorption and high singlet and triplet yields, which make them valuable photosensitizer for PDT applications.

Some previous papers reported that ZnPc derivatives functionalized with substituents such as polyoxyethylene, pyridyloxy, 4-pyridylmethyloxy and crown ether groups in peripheral and non-peripheral positions on the phthalocyanine ring which have compounds offered PDT properties due to their interesting photophysical properties [19–25].

One of the most important characteristic of a photosensitizing drug is the perfect balance between its hydrophobic and

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hydrophilic properties. Phthalocyanine skeletons are essentially hydrophobic due to intermolecular interactions between the macrocycles. The solubility of phthalocyanines can be improved by introduction of substituents on the periphery of the molecule, which increase the π -electron density and make solvation easier [18]. Some water-soluble phthalocyanine compounds have potential for use as photosensitizers in PDT since they can be injected directly into the bloodstream. The water solubility of these photosensitizers is an additional advantage despite the fact that the aggregation tendency in such polar medium, in particular, is very high [26]. Hydrophilic phthalocyanines are therefore important and potentially useful materials. A substantial number of water-soluble tetra- and octa-substituted phthalocyanines have been reported. The hydrophilic moieties which have been incorporated on the substituted by periphery of phthalocyanine ring include sulfonates [27], carboxylates [28], phosphanates [29], and quaternized amino groups [30–32]. Another type of water-soluble phthalocyanines contains hydrophilic groups as axial ligands coordinated to the central metal ion [33].

In this work, the synthesis, characterization and spectroscopic behaviour as well as photophysical (fluorescence quantum yields and lifetimes) and photochemical (singlet oxygen and photodegradation quantum yields) properties of new tetra- and octa-6-oxyquinoline substituted non-ionic (**5** and **6**) and quaternized ionic (**5a** and **6a**) zinc (II) phthalocyanine complexes (Fig. 1) are presented. The aim of our ongoing research is to synthesize water-soluble zinc (II) phthalocyanines to be used as potential PDT agents, since zinc (II) phthalocyanine complexes show good photophysical and photochemical properties for PDT studies.

BSA and human serum albumin (HSA) are major plasma proteins, which contribute significantly to physiological functions and display effective drug delivery roles [34,35], hence the investigation of binding of drugs with albumin is of interest. A spectroscopic investigation of the binding of the water-soluble zinc (II) phthalocyanine complexes (**5a** and **6a**) to BSA is also presented in this work.

2. Experimental

2.1. Materials

All reagents and solvents were of reagent grade quality and were obtained from commercial suppliers. 6-Hydroxyquinoline was purchased from Aldrich. 9,10-Antracenediyl-bis(methylene) dimalonic acid (ADMA) and 1,3-diphenylisobenzofuran (DPBF) were purchased from Fluka. All solvents were dried and purified as described by Perrin and Armarego [36]. 4-Nitrophthalonitrile [37], 1,2-dichlorophthalonitrile [38] were synthesized and purified according to well known literature.

2.2. Equipment

The IR spectra were recorded on a Perkin Elmer 1600 FT-IR spectrophotometer using KBr pellets. ^1H - and ^{13}C NMR spectra were recorded on a Varian Mercury 200 MHz spectrometer in CDCl_3 and DMSO-d_6 . Chemical shifts were reported (δ) relative to Me_4Si as internal standard. Mass spectra were measured on a Micro-mass Quatro LC/ULTIMA LC-MS/MS spectrometer. The elemental analyses were performed on a Costech ECS 4010 instrument. Melting points were measured on an electrothermal apparatus and were uncorrected. Absorption spectra in the UV-vis region were recorded with a Shimadzu 2001 UV spectrophotometer. Fluorescence excitation and emission spectra were recorded on a Varian Eclipse spectrofluorometer using 1 cm pathlength cuvettes at room temperature.

Photo-irradiations were done using a General Electric quartz line lamp (300 W). A 600 nm glass cut off filter (Schott) and a water filter were used to filter off ultraviolet and infrared radiations, respectively. An interference filter (Intor, 670 nm with a band width of 40 nm) was additionally placed in the light path before the sample. Light intensities were measured with a POWER MAX5100 (Molelectron detector incorporated) power meter.

2.3. Photophysical parameters

2.3.1. Fluorescence quantum yields and lifetimes

Fluorescence quantum yields (Φ_F) are determined by the comparative method (Eq. (1)) [39,40],

$$\Phi_F = \Phi_F(\text{Std}) \frac{F A_{\text{Std}} n^2}{F_{\text{Std}} A n_{\text{Std}}^2} \quad (1)$$

where F and F_{Std} are the areas under the fluorescence emission curves of the samples (**5**, **5a**, **6** and **6a**) and the standard, respectively. A and A_{Std} are the respective absorbances of the samples and standard at the excitation wavelengths, respectively. n^2 and n_{Std}^2 are the refractive indices of solvents used for the sample and standard, respectively. Unsubstituted ZnPc (in DMSO) ($\Phi_F = 0.20$) [41] was employed as the standard. The absorbance of the solutions at the excitation wavelength ranged between 0.04 and 0.05.

Natural radiative life times (τ_0) are determined using PhotochemCAD program which uses the Strickler–Berg equation [42]. The fluorescence lifetimes (τ_F) are evaluated using Eq. (2).

$$\Phi_F = \frac{\tau_F}{\tau_0} \quad (2)$$

2.4. Photochemical parameters

2.4.1. Singlet oxygen quantum yields

Singlet oxygen quantum yield (Φ_Δ) determinations are carried out using the experimental set-up described in literature [27]. Typically, a 3 mL portion of the respective unsubstituted, tetra- and octa-substituted zinc (II) phthalocyanine (**5**, **5a**, **6** and **6a**) solutions (absorbance ~ 1.0 at the irradiation wavelength) containing the singlet oxygen quencher was irradiated in the Q band region with the photo-irradiation set-up described in references [27]. Φ_Δ values were determined in air using the relative method with ZnPc (in DMSO) or $\text{ZnPcS}_{\text{mix}}$ (in aqueous media) as references. DPBF and ADMA were used as chemical quenchers for singlet oxygen in DMSO and aqueous media, respectively. Eq. (3) was employed for the calculations:

$$\Phi_\Delta = \Phi_\Delta^{\text{Std}} \frac{R I_{\text{abs}}^{\text{Std}}}{R^{\text{Std}} I_{\text{abs}}} \quad (3)$$

where Φ_Δ^{Std} is the singlet oxygen quantum yields for the standard ZnPc ($\Phi_\Delta^{\text{Std}} = 0.67$ in DMSO) [43] and $\text{ZnPcS}_{\text{mix}}$ ($\Phi_\Delta^{\text{Std}} = 0.45$ in aqueous media) [27], R and R_{Std} are the DPBF (or ADMA) photobleaching rates in the presence of the respective samples (**5**, **5a**, **6** and **6a**) and standards, respectively. I_{abs} and $I_{\text{abs}}^{\text{Std}}$ are the rates of light absorption by the samples and standards, respectively. To avoid chain reactions induced by quenchers (DPBF or ADMA) in the presence of singlet oxygen [44], the concentration of quenchers (DPBF or ADMA) was lowered to $\sim 3 \times 10^{-5}$ M. Solutions of sensitizer (absorbance = 1 at the irradiation wavelength) containing quencher (DPBF or ADMA) were prepared in the dark and irradiated in the Q band region using the setup described above. DPBF degradation at 417 nm and ADMA degradation at 380 nm were monitored. The light intensity 6.21×10^{15} photons $\text{s}^{-1} \text{cm}^{-2}$ was used for Φ_Δ determinations.

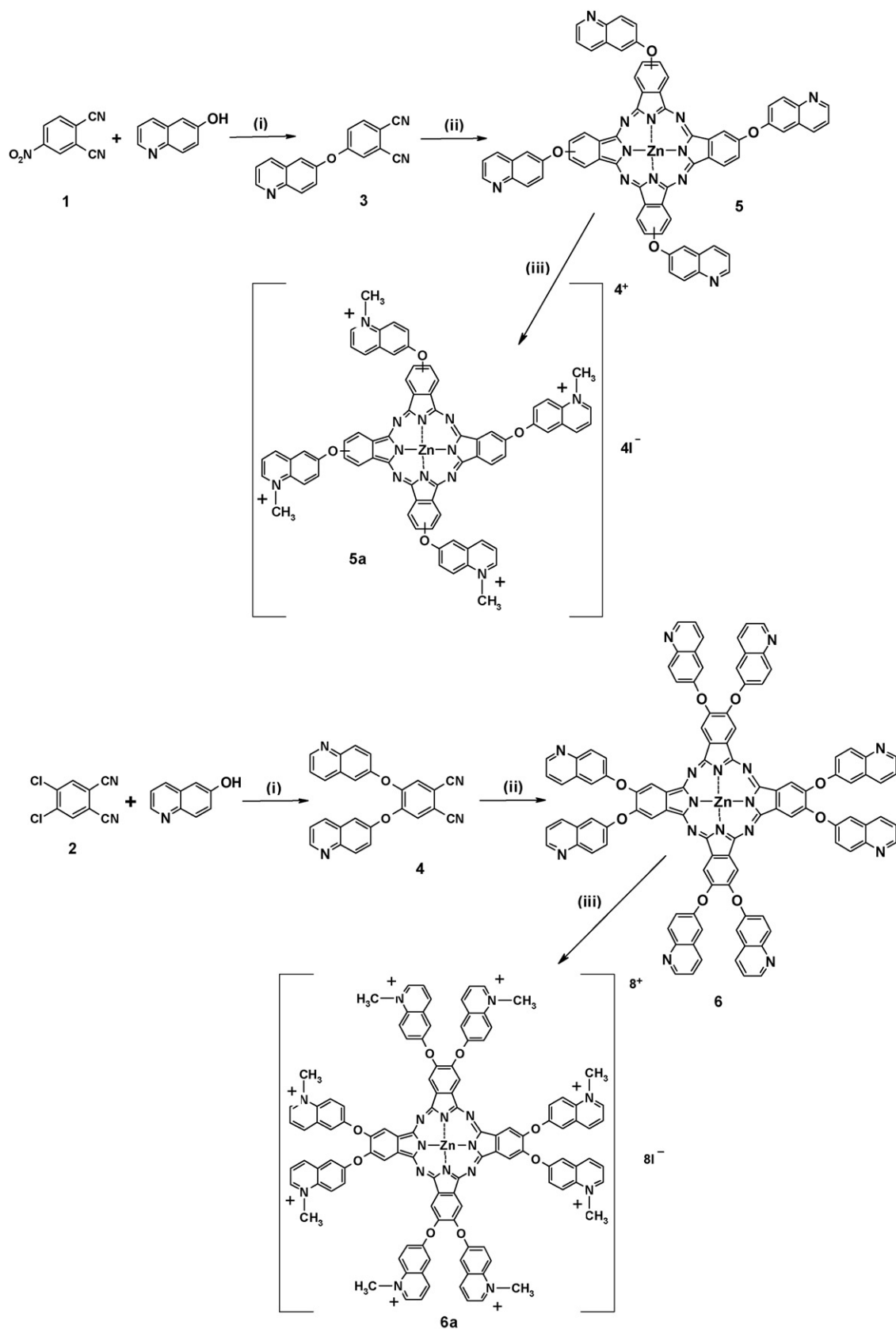


Fig. 1. Synthetic pathway for preparation of phthalocyanine complexes (**5**, **5a**, **6** and **6a**). (i) K_2CO_3 , N_2 , DMF, 50°C , 48 h. (ii) $\text{Zn}(\text{CH}_3\text{COO})_2$, DMAE, 175°C , 350 W. (iii) CHCl_3 , CH_3I , 5 h for compound **5a**, 8 h for compound **6a**.

2.4.2. Photodegradation quantum yields

Photodegradation quantum yield (Φ_d) determinations are carried out using the experimental set-up described in literature [27]. Photodegradation quantum yields were determined using Eq. (4),

$$\Phi_d = \frac{(C_0 - C_t) V N_A}{I_{\text{abs}} S t} \quad (4)$$

where C_0 and C_t are the samples (**5**, **5a**, **6** and **6a**) concentrations before and after irradiation respectively, V is the reaction volume, N_A the Avogadro's constant, S the irradiated cell area and t the irradiation time, I_{abs} is the overlap integral of the radiation source light intensity and the absorption of the samples. A light intensity of 2.17×10^{16} photons $\text{s}^{-1} \text{cm}^{-2}$ was employed for Φ_d determinations.

2.4.3. Binding of quaternized zinc (II) phthalocyanine derivatives to BSA

The binding of the quaternized zinc (II) phthalocyanine derivatives (**5a** and **6a**) to BSA was studied by spectrofluorometry at room temperature. A PBS solution of BSA (fixed concentration) was titrated with varying concentrations of the respective quaternized zinc (II) phthalocyanine solutions. BSA was excited at 280 nm and fluorescence recorded between 290 and 500 nm. The changes in BSA fluorescence intensity were related to quaternized phthalocyanine concentrations by the Stern–Volmer relationship (Eq. (5)):

$$\frac{F_0^{\text{BSA}}}{F^{\text{BSA}}} = 1 + K_{\text{SV}}^{\text{BSA}} [\text{PC}] \quad (5)$$

and $K_{\text{SV}}^{\text{BSA}}$ is given by Eq. (6):

$$K_{\text{SV}}^{\text{BSA}} = k_q \tau_F(\text{BSA}) \quad (6)$$

where F_0^{BSA} and F^{BSA} are the fluorescence intensities of BSA in the absence and presence of quaternized phthalocyanines (**5a** and **6a**), respectively; $K_{\text{SV}}^{\text{BSA}}$, the Stern–Volmer quenching constant; k_q , the bimolecular quenching constant; and τ_F (BSA), the fluorescence lifetime of BSA. τ_F (BSA) is known to be 10 ns [45–47], thus from the values of $K_{\text{SV}}^{\text{BSA}}$ obtained from the plots of $F_0^{\text{BSA}}/F^{\text{BSA}}$ versus [PC], the value of k_q may be determined (Eq. (6)).

2.5. Synthesis

2.5.1. Synthesis of 4-(quinolin-6-yloxy)phthalonitrile (**3**)

4-Nitrophthalonitrile (**1**) (1.19 g, 6.90 mmol) and 6-hydroxyquinoline (1.00 g, 6.90 mmol) were dissolved in dry dimethylformamide (DMF) (10 mL) at 50 °C under N_2 atmosphere. Potassium carbonate (2.38 g, 17.25 mmol) was added to the reaction solution in 8 portions every 15 min. The reaction mixture was heated for 48 h, then cooled to room temperature, and poured into ice-water (100 mL). After filtration under vacuum, the crude product was crystallized from ethanol. Yield: 1.14 g (61%), mp: 147–148 °C. IR (KBr pellet), $\nu_{\text{max}}/\text{cm}^{-1}$: 3077–3038 (Ar–H), 2232 (C≡N), 1624, 1594, 1565, 1498, 1487, 1324, 1280, 1249, 1213, 1166, 1138, 1088, 968, 880, 836, 756. ^1H NMR. (CDCl_3), (δ ppm): 8.97 (d, 1H, Ar–H), 8.20 (m, 2H, Ar–H), 7.79 (d, 1H, Ar–H), 7.52–7.44 (m, 3H, Ar–H), 7.37–7.32 (m, 2H, Ar–H). ^{13}C NMR. (CDCl_3), (δ ppm): 163.32, 153.54, 152.70, 149.28, 137.54, 134.80, 131.07, 125.29, 124.18, 123.98, 123.77, 119.90, 118.59, 117.20, 116.77, 111.55, 107.46. MS (ES^+), (m/z): 272 [M+H] $^+$.

2.5.2. Synthesis of 2,9(10),16(17),23(24)-tetrakis-(quinolin-6-yloxy)phthalocyaninato zinc (II) (**5**)

4-(Quinolin-6-yloxy)phthalonitrile (**3**) (0.400 g, 1.47 mmol) and anhydrous $\text{Zn}(\text{CH}_3\text{COO})_2$ (0.068 g, 0.37 mmol) were ground together in a microwave oven and 2-(dimethylamino)ethanol (DMAE) (3 mL) was added. The reaction mixture was irradiated in

microwave reaction oven at 175 °C, 350 W for 10 min. After cooling to room temperature, ethanol (60 mL) was added. The precipitated green solid product was filtered off, and then dried. The obtained green product was purified by the column chromatography over aluminium oxide using chloroform:methanol (100:2) as solvent system. Yield: 0.112 g (53%). IR (KBr pellet) $\nu_{\text{max}}/\text{cm}^{-1}$: 3083 (Ar–H), 1607, 1593, 1499, 1462, 1376, 1322, 1259, 1223, 1089, 1045, 963, 833, 748. ^1H NMR. ($\text{DMSO}-d_6$), (δ ppm): 8.87 (m, 4H, Ar–H), 8.29 (d, 4H, Ar–H), 8.09–7.86 (m, 8H, Ar–H), 7.69–7.36 (m, 20H, Ar–H). Calc. for $\text{C}_{68}\text{H}_{36}\text{N}_{12}\text{O}_4\text{Zn}$: C 70.99, H 3.15, N 14.61; Found: C 71.43, H 3.34, N 14.16. MS (ES^+), (m/z): Calc. 1150; Found: 1151 [M+H] $^+$.

2.5.3. Synthesis of quaternized 2,9(10),16(17),23(24)-tetrakis-(quinolin-6-yloxy)phthalocyaninato zinc (II) (**5a**)

Compound **5** (0.050 g, 0.043 mmol) was dissolved in chloroform (4 mL) and methyl iodide (0.030 g, 0.21 mmol) was added to this solution. The reaction mixture was stirred under reflux for 5 h. After cooling to room temperature, the green precipitate was filtered off, washed with ethanol, acetone, diethyl ether, chloroform, and then dried. Yield: 0.048 g (65%). IR (KBr pellet) $\nu_{\text{max}}/\text{cm}^{-1}$: 3010 (Ar–H), 2923–2851 (Aliph. C–H), 1597, 1526, 1481, 1464, 1389, 1332, 1266, 1240, 1088, 1045, 965, 941, 746. Calc. for $\text{C}_{72}\text{H}_{48}\text{I}_4\text{N}_{12}\text{O}_4\text{Zn}$: C 50.33, H 2.82, N 9.78; Found: C 49.38, H 2.95, N 9.47. MS (ES^+), (m/z): Calc. 1718; Found: 1658 [M-4CH $_3$] $^+$.

2.5.4. Synthesis of 4,5-bis-(quinolin-6-yloxy)phthalonitrile (**4**)

4,5-Dichlorophthalonitrile (**2**) (1.36 g, 6.89 mmol) and 6-hydroxyquinoline (2.00 g, 13.79 mmol) were dissolved in dry DMF (10 mL) at 50 °C under N_2 atmosphere. Potassium carbonate (2.85 g, 20.67 mmol) was added to the reaction solution in 8 portions every 15 min. The reaction mixture was heated for 48 h, then cooled to room temperature, and poured into ice-water (80 mL). After filtration under vacuum, the crude product was crystallized from ethanol. Yield: 1.22 g (43%), mp: 152–153 °C. IR (KBr pellet), $\nu_{\text{max}}/\text{cm}^{-1}$: 3084–3025 (Ar–H), 2235 (C≡N), 1648, 1620, 1597, 1562, 1499, 1462, 1396, 1324, 1295, 1211, 1151, 1136, 1070, 958, 877, 835, 799. ^1H NMR. ($\text{DMSO}-d_6$), (δ ppm): 8.83 (d, 2H, Ar–H), 8.28 (d, 2H, Ar–H), 8.11 (s, 2H, Ar–H), 8.03 (d, 2H, Ar–H), 7.62–7.49 (m, 6H, Ar–H). ^{13}C NMR. ($\text{DMSO}-d_6$), (δ ppm): 152.72, 150.73, 149.73, 144.96, 135.36, 131.34, 128.55, 126.31, 122.15, 121.91, 115.16, 113.89, 111.50. MS (ES^+), (m/z): 415 [M+H] $^+$.

2.5.5. Synthesis of 2,3,9,10,16,17,23,24-octakis-(quinolin-6-yloxy)phthalocyaninato zinc (II) (**6**)

4,5-Bis-(quinolin-6-yloxy)phthalonitrile (**4**) (0.50 g, 1.20 mmol) and anhydrous $\text{Zn}(\text{CH}_3\text{COO})_2$ (0.056 g, 0.30 mmol) were ground together in a microwave oven and DMAE (3 mL) was added. The reaction mixture was irradiated in microwave reaction oven at 175 °C, 350 W for 12 min. After cooling to room temperature, ethanol (80 mL) was added. The precipitated green solid product was filtered off, and then dried. The green product was purified by the column chromatography over aluminium oxide using chloroform:methanol (100:3) as solvent system. Yield: 0.310 g (60%). IR (KBr pellet) $\nu_{\text{max}}/\text{cm}^{-1}$: 3054 (Ar–H), 1621, 1598, 1500, 1446, 1401, 1377, 1323, 1271, 1214, 1177, 1145, 1114, 1088, 1027, 961, 920, 832, 746. ^1H NMR. (CDCl_3), (δ ppm): 8.82 (m, 8H, Ar–H), 8.06 (m, 16H, Ar–H), 7.48–7.36 (m, 32H, Ar–H). Calc. for $\text{C}_{104}\text{H}_{56}\text{N}_{16}\text{O}_8\text{Zn}$: C 72.49, H 3.28, N 13.01; Found: C 72.88, H 3.57, N 12.79. MS (ES^+), (m/z): Calc. 1723; Found: 1746 [M+Na] $^+$.

2.5.6. Synthesis of quaternized 2,3,9,10,16,17,23,24-octakis-(quinolin-6-yloxy)phthalocyaninato zinc (II) (**6a**)

Compound **6** (0.10 g, 0.058 mmol) was dissolved in chloroform (6 mL) and methyl iodide (0.081 g, 0.58 mmol) was added to this solution. The reaction mixture was stirred under reflux for 8 h. After

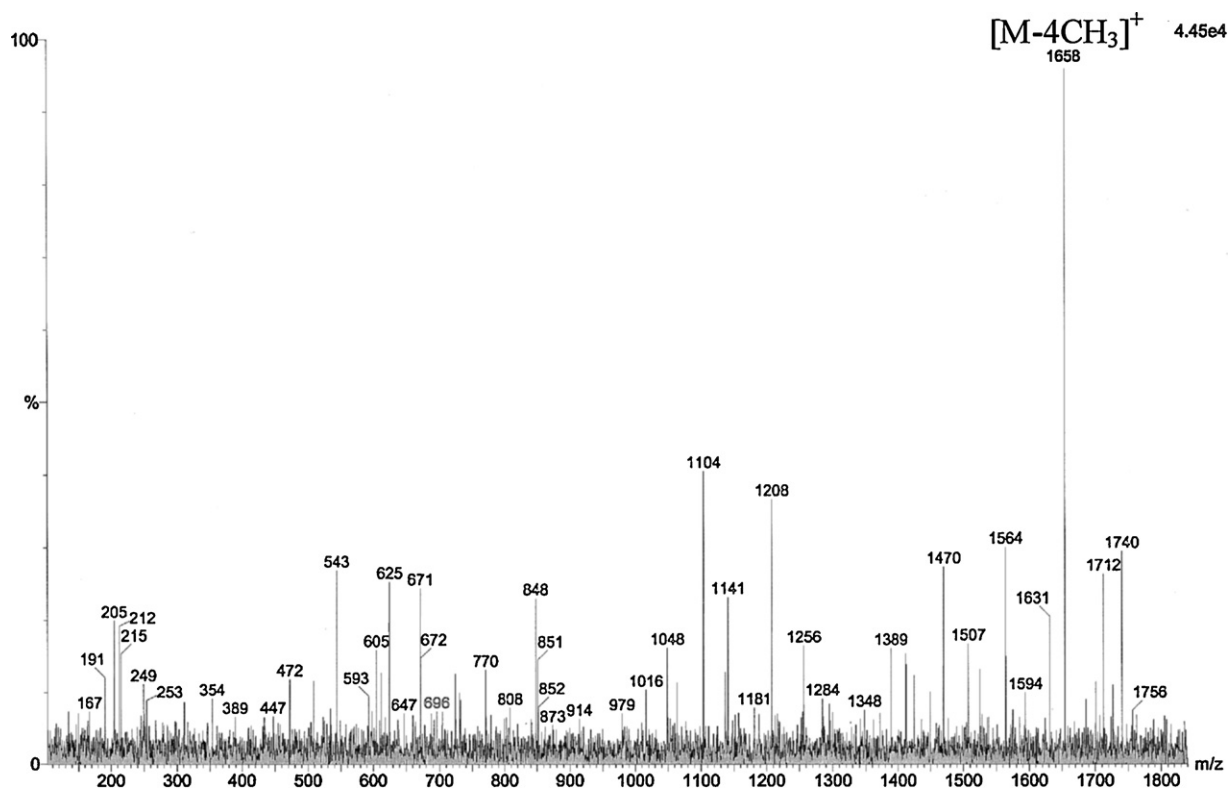


Fig. 2. Mass spectrum of complex **5a**.

cooling to room temperature, the green precipitate was filtered off, washed with ethanol, acetone, diethyl ether and chloroform, and then dried. Yield: 0.119 g (72%). IR (KBr pellet) $\nu_{\max}/\text{cm}^{-1}$: 3076 (Ar–H), 2923–2851 (Aliph. C–H), 1621, 1596, 1522, 1445, 1385, 1270, 1231, 1083, 1028, 960. Calc. for $C_{112}H_{80}I_8N_{16}O_8Zn$: C 47.06, H 2.82, N 7.84; Found: C 46.74, H 2.99, N 7.70. MS (ES^+), m/z : Calc. 2858; Found: 2859 $[M+H]^+$.

3. Results and discussion

3.1. Synthesis and characterization

The synthetic procedure of the phthalocyanine complexes (**5** and **6**) and their quaternized derivatives (**5a** and **6a**) is given in Fig. 1. 6-Oxyquinoline substituted phthalonitrile derivatives (**3** and **4**) were synthesized through base-catalyzed aromatic displacement of 4-nitrophthalonitrile (**1**) and 4,5-dichlorophthalonitrile (**2**) with 6-hydroxyquinoline using K_2CO_3 as the base in dry DMF. The reactions were carried out at 50°C under N_2 atmosphere for 48 h. Cyclotetramerization of the phthalonitrile derivatives (**3** and **4**) to the tetra- and octa-substituted zinc (II) phthalocyanines (**5** and **6**) were accomplished in the presence of anhydrous $Zn(CH_3COO)_2$ in DMAE by using microwave irradiation and the crude product was purified column chromatography using alumina filled column. Tetra- and octa-cationic zinc (II) phthalocyanines (**5a** and **6a**) were obtained from the reaction of corresponding zinc phthalocyanines (**5** and **6**) with methyl iodide in chloroform. The structures of the target compounds were confirmed using IR, 1H NMR, ^{13}C NMR spectroscopy and mass spectra. The analyses are consistent with the predicted structures as shown in Section 2.

The IR spectra clearly indicated the formation of compounds (**3**) and (**4**) with the appearance of absorption bands at 2232 cm^{-1} ($C\equiv N$), 1624 cm^{-1} ($C=N$) for compound (**3**) and 2235 cm^{-1} ($C\equiv N$), 1620 cm^{-1} ($C=N$) for compound (**4**). In the 1H NMR spectra of com-

pounds **3** and **4** the aromatic protons appeared at 8.97 (d), 8.20 (m), 7.79 (d), 7.52–7.44 (m), 7.37–7.32 (m) ppm for compound **3** and 8.83 (d), 8.28 (d), 8.11 (s), 8.03 (d), 7.62–7.49 (m) ppm for compound **4**. The ^{13}C NMR spectra of compounds **3** and **4** indicated aromatic carbon atoms between at 163.32–107.46 and 152.72–111.50 ppm, respectively. Also nitrile carbon atoms for compounds **3** and **4** were observed 116.77, 111.55 and 113.89 ppm, respectively. In the mass spectra of compounds **3** and **4** the presence of molecular ion peaks at $m/z=272$ $[M+H]^+$ and 415 $[M+H]^+$ respectively, confirmed the proposed structures.

Cyclotetramerization of the dinitrile derivatives (**3** and **4**) to the zinc (II) phthalocyanines (**5** and **6**) were confirmed by the disappearance of the sharp $C\equiv N$ vibration of 2232 and 2235 cm^{-1} , respectively. The 1H NMR spectra of tetra- and octa-substituted zinc (II) phthalocyanines (**5** and **6**) were obtained as expected. The 1H NMR spectrum of tetra-substituted zinc (II) phthalocyanine (**5**) indicated the aromatic protons at 8.87, 8.29, 8.09–7.86, 7.69–7.36 ppm. Also, the 1H NMR spectrum of octa-substituted zinc (II) phthalocyanine (**6**) indicated the aromatic protons at 8.82, 8.06, 7.48–7.36 ppm. The mass spectra of phthalocyanine compounds showed molecular ion peaks at $m/z=1151$ $[M+H]^+$ for **5**, 1746 $[M+Na]^+$ for **6** support the proposed formula for these compounds.

Quaternized tetra- and octa-substituted zinc phthalocyanines (**5a** and **6a**) are soluble in water, DMF and DMSO. No major change in the IR spectra was found after quaternization. The mass spectra of quaternized tetra- and octa-substituted zinc (II) phthalocyanines (**5a** and **6a**) confirmed the proposed structure, with the molecular ion being easily identified at 1658 $[M-4CH_3]^+$ for **5a**, 2859 $[M+H]^+$ for **6a** (Fig. 2 for complex **5a** as an example).

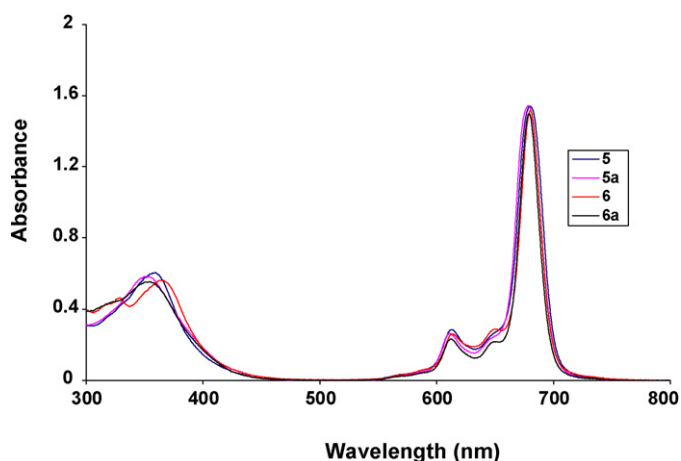
3.2. Ground state electronic absorption and fluorescence spectra

The electronic spectra of the studied zinc (II) phthalocyanine complexes showed characteristic absorption in the Q band region at around 680 nm in DMSO, Table 1. The B-bands were observed at

Table 1

Absorption, excitation, emission, photophysical and photochemical data for unsubstituted, tetra- and octa-substituted zinc (II) phthalocyanine complexes in DMSO and PBS.

Comp.	Solvent	Q band, λ_{\max} (nm)	Log ϵ	Excitation, λ_{Ex} (nm)	Emission, λ_{Em} (nm)	Stokes shift, Δ_{Stokes} (nm)	Φ_{F}	τ_{F} (ns)	τ_0 (ns)	k_{F}^{a} (s^{-1}) ($\times 10^8$)	Φ_{d} ($\times 10^{-5}$)	Φ_{Δ}
5	DMSO	680	5.24	680	691	11	0.15	1.37	7.74	1.29	0.68	0.56
5a	DMSO	678	5.20	678	688	10	0.02	0.13	6.57	1.52	0.54	0.13
	PBS	687, 640	4.62, 4.69	–	–	–	–	–	–	–	3.64	0.07
6	DMSO	680	5.16	680	689	9	0.17	1.64	9.67	1.03	1.75	0.69
6a	DMSO	681	5.27	680	690	9	0.003	0.018	6.12	1.63	0.27	0.07
	PBS	665, 636	4.74, 4.58	–	–	–	–	–	–	–	2.05	0.03
ZnPc ^b	DMSO	672	5.14	672	682	10	0.20 ^c	1.22	6.80	1.47	2.61	0.67

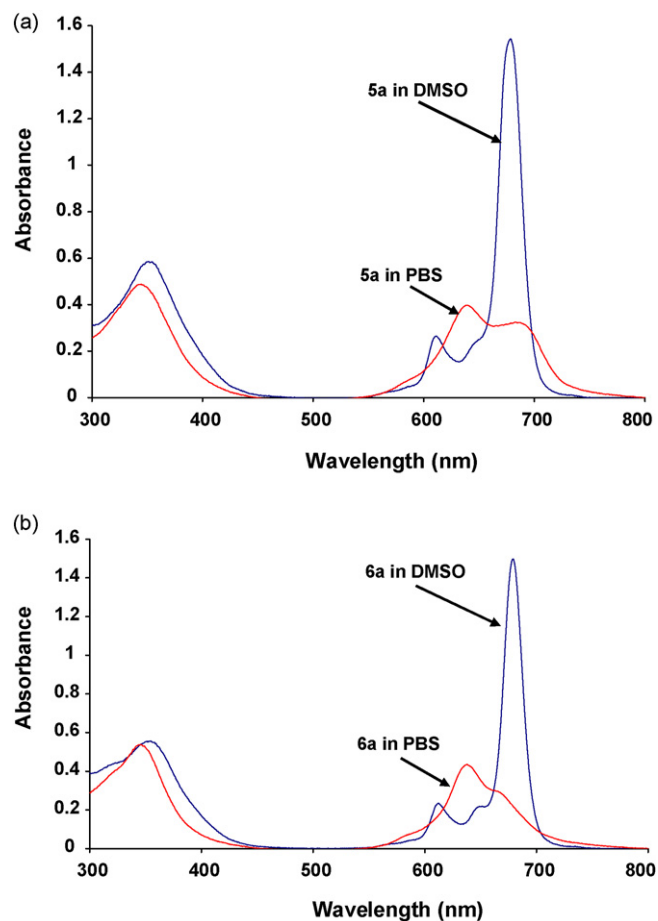
^a k_{F} is the rate constant for fluorescence. Values calculated using $k_{\text{F}} = \Phi_{\text{F}}/\tau_{\text{F}}$.^b Ref. [19].^c Ref. [41].**Fig. 3.** Absorption spectra of tetra- and octa-substituted zinc (II) phthalocyanines complexes (**5**, **5a**, **6** and **6a**) in DMSO. Concentration = 1×10^{-5} M.

around 350 nm (Fig. 3). The spectra showed monomeric behaviour evidenced by a single (narrow) Q band, typical of metallated phthalocyanine complexes in DMSO [48]. In DMSO, the Q bands were observed at: 680 (**5**), 678 (**5a**), 680 (**6**) and 681 (**6a**), Table 1. The red-shifts were observed for zinc (II) phthalocyanine complexes following substitution (the Q band for the unsubstituted ZnPc was 672 nm). The B-bands are broad due to the superimposition of the B_1 and B_2 bands in the 350 nm region. In PBS, the absorption spectra of quaternized complexes (**5a** and **6a**) showed co-facial aggregation, as evidenced by the presence of two non-vibrational peaks in the Q band region, Fig. 4a and b. The lower energy (red-shifted) bands at 687 nm for **5a** and 665 nm for **6a** were due to the monomeric species, while the higher energy (blue shifted) bands at 640 nm for **5a**, and 636 nm for **6a** were due to the aggregated species.

Aggregation is usually depicted as a coplanar association of rings progressing from monomer to dimer and higher order complexes. It is dependent on the concentration, nature of the solvent, nature of the substituents, complexed metal ions and temperature [49]. In the aggregated state the electronic structure of the complexed phthalocyanine rings are perturbed resulting in alternation of the ground and excited state electronic structures [50]. In this study, the aggregation behaviour of the zinc (II) phthalocyanine complexes (**5**, **5a**, **6** and **6a**) was investigated at different concentrations in DMSO (Fig. 5, for complex **6a** as an example). As the concentration was increased, intensity of absorption for the Q band also increased and there were no new bands (normally blue shifted) observed due to the aggregated species. The studied zinc (II) phthalocyanine complexes (**5**, **5a**, **6** and **6a**) did not

show aggregation in DMSO. Beer–Lambert law was obeyed for all of these compounds in DMSO for the concentrations ranging from 1.4×10^{-5} to 4×10^{-6} M.

Fig. 6 shows fluorescence emission, absorption and excitation spectra of zinc (II) phthalocyanine complexes (Fig. 6a for complex **6** and Fig. 6b for complex **6a** in DMSO as examples). All non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) showed similar fluorescence behaviour in DMSO (Fig. 6a for complex **6** as an example). For ionic zinc (II) complexes (**5a** and **6a**), the quaternization of the zinc (II) phthalocyanine complexes caused decreasing for fluorescence emission of the studied zinc (II) phthalocyanine complexes (Fig. 6b for complex **6a** as an example). Fluorescence emission peaks were

**Fig. 4.** Absorption spectra of: (a) tetra-substituted quaternized zinc (II) phthalocyanine (**5a**) and (b) octa-substituted quaternized zinc (II) phthalocyanine (**6a**) in DMSO and PBS. Concentration = 1×10^{-5} M.

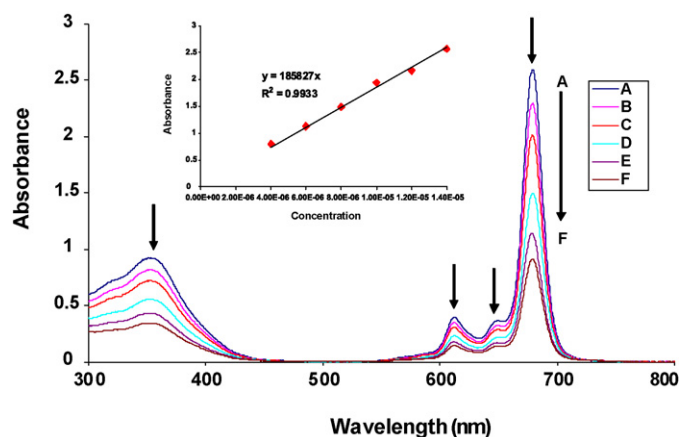


Fig. 5. Aggregation behaviour of **6a** in DMSO at different concentrations: 14×10^{-6} (A), 12×10^{-6} (B), 10×10^{-6} (C), 8×10^{-6} (D), 6×10^{-6} (E), 4×10^{-6} (F) M (inset: plot of absorbance versus concentration).

observed at 691 nm for **5**, 688 nm for **5a**, 689 nm for **6** and 690 nm for **6a** in DMSO (Table 1). The studied quaternized zinc (II) phthalocyanine complexes did not show fluorescence emission in PBS. The observed Stokes shifts (Table 1) were typical of MPc complexes. The excitation spectra were similar to absorption spectra and both had mirror images of the fluorescent spectra for all zinc (II) phthalocyanine complexes in DMSO (Fig. 6). The proximity of the wavelength of each component of the Q band absorption to the Q band maxima of the excitation spectra for all zinc (II) phthalocyanine complexes suggested that the nuclear configurations of the ground and excited states were similar and not affected by excitation in DMSO.

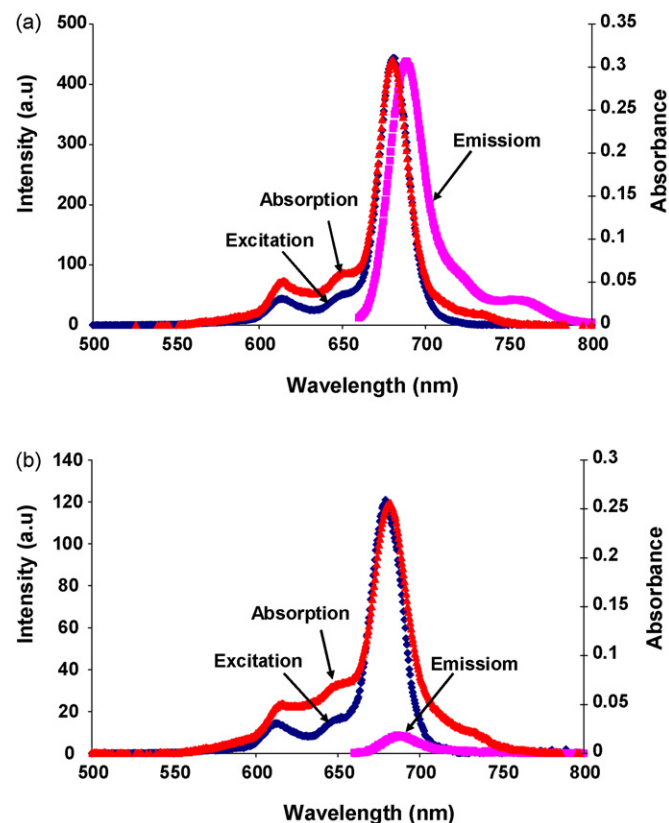


Fig. 6. Absorption, excitation and emission spectra of: (a) **6** in DMSO and (b) **6a** in DMSO. Excitation wavelengths: 650 nm.

3.3. Fluorescence lifetimes and quantum yields

The fluorescence quantum yields (Φ_F) for non-ionic (**5** and **6**) and for quaternized ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in DMSO were given in Table 1. The Φ_F values of studied non-ionic zinc (II) phthalocyanine complexes are typical of zinc (II) phthalocyanine complexes [19,20,51,52].

The Φ_F values of the substituted non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) were slightly lower as compared to unsubstituted zinc (II) phthalocyanine complex in DMSO. The Φ_F values of the quaternized ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) were lower than that of unsubstituted zinc (II) phthalocyanine complex in DMSO, which implied that the quaternization of the zinc (II) phthalocyanine complexes certainly results in fluorescence quenching. Quaternized cationic complexes (**5a** and **6a**) showed lower Φ_F values with respect to the corresponding non-ionic complexes (**5** and **6**) in DMSO. The lower values for quaternized zinc phthalocyanine complexes (**5a** and **6a**) were ascribed to the phenomenon of Photoinduced Electron Transfer (PET). Masking of the nitrogen lone pair electrons (as in **5a** and **6a**) prevents the nitrogen lone pair from participating in PET, and causes a quench the fluorescence of the ZnPc moiety.

Fluorescence lifetime (τ_F) refers to the average time a molecule stays in its excited state before fluorescing, and its value is directly related to that of Φ_F ; i.e. the longer the lifetime, the higher the quantum yield of fluorescence. Any factor that shortens the fluorescence lifetime of a fluorophore indirectly reduces the value of Φ_F . Such factors include internal conversion and intersystem crossing. As a result, the nature and the environment of a fluorophore determine its fluorescence lifetime. τ_F values (Table 1) were calculated using the Strickler–Berg equation. The τ_F values of the substituted non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) were higher to unsubstituted zinc (II) phthalocyanine complex in DMSO. The τ_F values of the substituted quaternized ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) were lower to unsubstituted zinc (II) phthalocyanine complex in DMSO, suggesting more quenching by quaternization of the zinc (II) phthalocyanine complexes. However the τ_F values were typical for non-ionic zinc (II) phthalocyanine complexes in DMSO [19,20,51,52].

The natural radiative lifetime (τ_0) and the rate constants for fluorescence (k_F) values were also shown in Table 1. The τ_0 values of the substituted non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) were also higher to substituted quaternized ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in DMSO. The k_F values of the substituted non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) were lower to substituted quaternized ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in DMSO.

3.4. Singlet oxygen quantum yields

Energy transfer between the triplet state of photosensitizers and ground state molecular oxygen leads to the production of singlet oxygen. There is a necessity of high efficiency of transfer of energy between excited triplet state of MPc and ground state of oxygen to generate large amounts of singlet oxygen, essential for PDT.

The Φ_Δ values were determined using a chemical method (DPBF in DMSO and ADMA in aqueous solution). The disappearance of quenchers (DPBF or ADMA) was monitored using UV–vis spectrophotometer (Fig. 7 using DPBF for complex **5** in DMSO as an example). Many factors are responsible for the magnitude of the determined quantum yield of singlet oxygen including; triplet excited state energy, ability of substituents and solvents to quench the singlet oxygen, the triplet excited state lifetime and the efficiency of the energy transfer between the triplet excited state and the ground state of oxygen. There was no change in the Q band intensity during the Φ_Δ determinations, confirming that com-

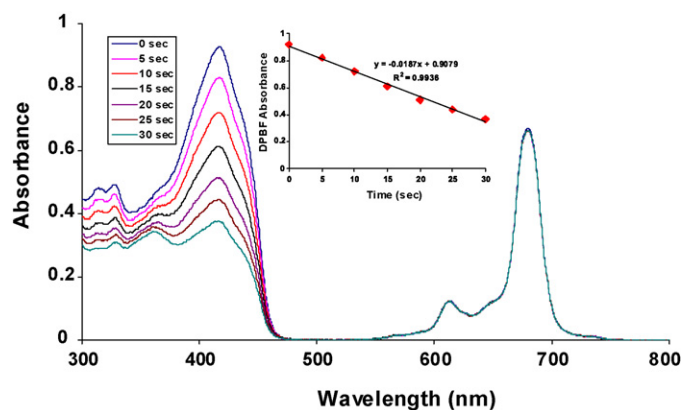


Fig. 7. A typical spectrum for the determination of singlet oxygen quantum yield of **5** in DMSO using DPBF as a singlet oxygen quencher. Concentration = 4×10^{-6} M (inset: plots of DPBF absorbance versus time).

plexes were not degraded during singlet oxygen studies (Fig. 7 as an example for complex **5**). Table 1 showed that the values of Φ_{Δ} were higher for substituted non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) when compared to respective substituted quaternized ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in DMSO. The quaternization of the zinc (II) phthalocyanine complexes caused the decreasing of the Φ_{Δ} values in DMSO.

Table 1 shows that lower Φ_{Δ} values were observed in PBS (which is mainly water) solutions as compared to in DMSO. The low Φ_{Δ} in water compared to other solvents such as deuterated water and DMSO was explained [41] by the fact that singlet oxygen absorbs at 1270 nm, and water, which absorbs around this wavelength has a great effect on singlet oxygen lifetime, while DMSO which exhibits little absorption in this region has longer singlet oxygen lifetimes than water, resulting in large Φ_{Δ} values in DMSO. Low singlet oxygen values of quaternized phthalocyanine complexes (**5a** and **6a**) in PBS could also be due to aggregation.

3.5. Photodegradation studies

Degradation of the molecules under irradiation can be used to study their stability and this is especially important for those molecules intended for use in photocatalysis. The collapse of the absorption spectra without any distortion of the shape confirms clean photodegradation not associated with phototransformation into different forms of MPC absorbing in the visible region. The spectral changes observed for all the studied complexes (**5**, **5a**, **6** and **6a**) during confirmed photodegradation occurred without phototransformation (Fig. 8 as an example for complex **6**).

All the studied zinc (II) phthalocyanine complexes showed about the same stability with Φ_d of the order of 10^{-5} in DMSO, Table 1. Stable zinc phthalocyanine complexes show Φ_d values as low as 10^{-6} and for unstable molecules, values of the order of 10^{-3} have been reported [53]. Studied zinc (II) phthalocyanine complexes seemed to show similar Φ_d values and stability with other zinc (II) phthalocyanine complexes. Table 1 shows that the lower Φ_d values were observed for the studied quaternized ionic zinc (II) phthalocyanine complexes as compared to for the studied non-ionic zinc (II) phthalocyanine complexes. The quaternization of the zinc (II) complexes caused the increasing of the stability of the zinc (II) phthalocyanine complexes in DMSO. The Φ_d values for quaternized ionic zinc (II) phthalocyanine complexes were higher in PBS solution than in DMSO. These complexes were more stable in DMSO than in PBS.

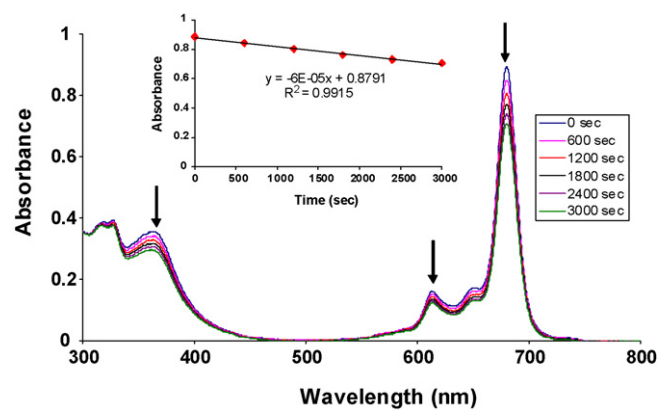


Fig. 8. The photodegradation of **6** in DMSO showing the disappearance of the Q band at 10 min intervals (inset: plot of Q band absorbance versus time).

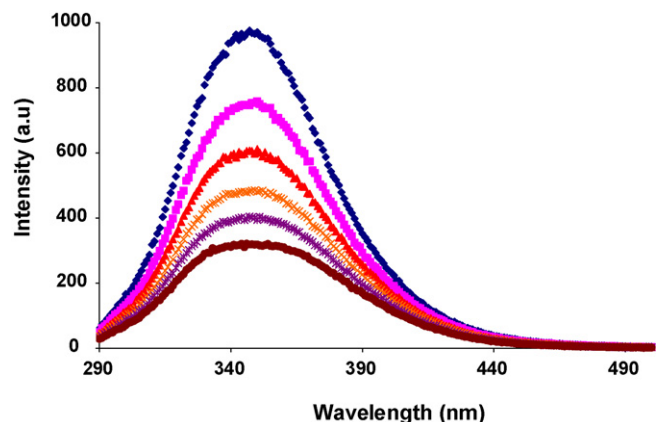


Fig. 9. Fluorescence emission spectral changes of BSA on addition of varying concentrations of **5a** in PBS. [BSA] = 3.00×10^{-5} M, [5a] varies from 0 to 8.30×10^{-6} M. Excitation wavelength = 280 nm.

3.6. Interaction of quaternized ionic Zn (II) phthalocyanine complexes with BSA

Fig. 9 shows the fluorescence emission spectra of BSA in the presence of different concentrations of **5a** in PBS as an example. The BSA fluorescence at 348 nm is mainly attributable to tryptophan residues in the macromolecule. BSA and the respective quaternized ionic phthalocyanine complexes exhibited reciprocated fluorescence quenching on one another; hence it was possible to determine Stern–Volmer quenching constants (K_{SV}). The slope of the plots shown at Fig. 10 gave K_{SV} values and listed in Table 2, suggested that BSA fluorescence quenching was more effective for quaternized octa-substituted zinc (II) phthalocyanine complex (**6a**) than quaternized tetra-substituted phthalocyanine complex (**5a**) in PBS. Using the approximate fluorescence lifetime of BSA (10 ns) [43,44], the bimolecular quenching constant (k_q) was determined (Eq. (6)). These values were of the order of $10^{13} \text{ M}^{-1} \text{ s}^{-1}$, which exceeded the proposed value of $10^{10} \text{ M}^{-1} \text{ s}^{-1}$ for diffusion-controlled (dynamic) quenching (according to the Einstein–Smoluchowski approximation at room

Table 2

Binding and fluorescence quenching data for interaction of BSA with quaternized zinc (II) phthalocyanine complexes (**5a** and **6a**) in PBS.

Compound	$K_{SV}^{BSA} (\times 10^5 \text{ M}^{-1})$	$k_q (\times 10^{13} \text{ s}^{-1})$
5a	2.14	2.14
6a	2.98	2.99

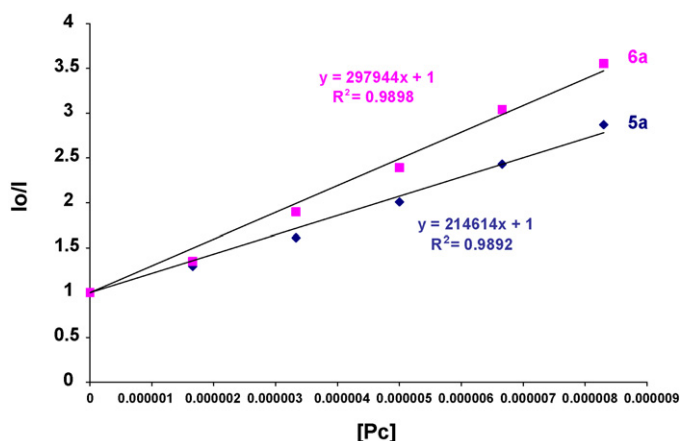


Fig. 10. Stern–Volmer plots of quaternized tetra- and octa-substituted zinc (II) phthalocyanines quenching of BSA in PBS. [BSA] = 3.00×10^{-5} M, [Pc] varies from 0 to 8.30×10^{-6} M.

temperature) [54]. This was also an indication that the mechanism of BSA quenching by quaternized phthalocyanine complexes (**5a** and **6a**) was not diffusion-controlled (i.e., not dynamic quenching, but static quenching). The k_q value was larger for quaternized octa-substituted phthalocyanine complex (**6a**) than quaternized tetra-substituted phthalocyanine complex (**5a**) in PBS.

4. Conclusion

In conclusion, this work has described the synthesis, spectral, photophysical and photochemical properties of new peripherally tetra- and octa-6-oxoquinoline substituted non-ionic and quaternized ionic zinc (II) phthalocyanine complexes. The effect of quaternization on these properties was presented. It was shown that quaternization imparted water solubility and enhanced the photophysical and photochemical value of the quaternized phthalocyanine complexes. Solvent effect (DMSO or PBS) on the photophysical and photochemical properties of the quaternized derivative was determined. The non-ionic and ionic zinc (II) phthalocyanine complexes were found to be monomeric in DMSO. The ionic complexes showed aggregation in PBS. The studied non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) showed similar fluorescence behaviour with MPCs. The ionic Zn (II) phthalocyanine complexes showed less fluorescence emission in DMSO and they were not fluorescence in PBS. The Φ_F values of the non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) were higher than that of ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in DMSO. The Φ_Δ values were higher for the non-ionic zinc (II) phthalocyanine complexes (**5** and **6**) than ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in DMSO. The Φ_Δ values were higher in DMSO than that of ionic zinc (II) phthalocyanine complexes (**5a** and **6a**) in PBS. This study reveals that the water-soluble derivatives bind strongly to serum albumin; hence they can easily be transported in the blood. After injection into the blood stream, these molecules will have to encounter serum albumin, which presents a justification for their BSA binding study.

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