New soluble amidoamine substituted phthalocyanines: synthesis, characterization, and investigation of their solution properties

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Abstract: The synthesis of tetraaminopropylamid substituted phthalocyanines was targeted to prepare enhanced soluble phthalocyanines in common solvents from hydrophobic to hydrophilic that bore nonionic groups on their periphery. Metal-free (H_2Pc) and metallophthalocyanines (Zn(II) (ZnPc), Cu(II) (CuPc) and Co(II) (CoPc)) were prepared and characterized by UV-Vis, FT-IR, and mass spectroscopies. The ^1H NMR spectra were recorded for the diamagnetic phthalocyanine species H_2Pc and ZnPc. The phthalocyanines showed sufficient solubility in common organic solvents such as dimethyl sulfoxide, tetrahydrofuran, and ethanol. However, methanol was not a good solvent for CuPc and H_2Pc. Solubility and aggregation studies of H_2Pc and ZnPc were performed in different solvents and different concentrations in DMF. The solubility in water was also examined by altering pH to exhibit solubility characteristic in polar solvents for H_2Pc and ZnPc.

Key words: Synthesis, soluble phthalocyanines, aggregation value, tetra substituted phthalocyanines

1. Introduction

Phthalocyanine derivatives (Pcs) are currently of great interest due to their chemical and physical properties as well as their various applications in recent years.[1] They have been employed in various technological applications such as in photo-conversion readwrite compact discs, non-linear optics, liquid crystals, dye-sensitized solar cells, oxidation or reduction catalysts, nanotechnology, medicine, and photosensitizers for photodynamic therapy (PDT).[2−13] These applications exploit the unique optical properties, and high thermal and chemical stabilities of Pcs.[14] UV-Vis and fluorescent spectroscopies were used in the characterization of the excited states of Pcs and their analogs. Pcs are known for their characteristic B and Q bands, which are observed at 300–400 nm and 600–700 nm in UV-Vis spectra, respectively.[15]

Amino Pcs bearing corresponding reactive amino groups as substituents are desired compounds due to their improved solubility. Derivatization from the reactive amino functionalities makes them important intermediates and convenient photosensitizers for PDT having the ability of strong interaction or bonding with the corresponding biological molecules. Additionally, introduction of amino groups increases the water solubility of Pc macrocycles when they are quaternized. Therefore, there have been considerable efforts to synthesize such compounds that include amino groups.[16,17] Fashina et al. have described the process of interaction of silica nanoparticles (containing amino groups) with zinc phthalocyanine (ZnPc) complexes in their recent studies.[18]

Many methods have been reported to convert tertiary amine compounds to zwitterionic or cationic moi-

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eties by using 1,3-propanesultone, 2-(phenylsulfonyl)-3- phenyloxaziridine, hydrogen peroxide, meta chloroper-benzoic acid, methyl iodide, etc.[19−24] Brault et al. investigated zwitterionic carboxybetaine polymer (pCB) coated substrates as an array surface platform for the sensitive detection of target analytes from undiluted human blood plasma.[25] Sulfobetaine and betaine type zwitterionic derivatives, having in general quaternized alkyl amine moieties, have been studied intensively for reducing nonspecific protein and surface chemistry.[26] Amidoamine and imidazoline derivatives are suggested as exhibiting an outstanding combination of surfactant characteristics. They are also well tolerated by human tissue and exhibit exceptionally low ocular irritation and oral toxicity.[27−29] Amides and amidoamines of fatty acids and polyamines also have extremely good oil solubility, and so these products are used as typical corrosion inhibitors in high dosage despite their poor biodegradability.[30] Polyamines play an important biological role in cell growth and bind to phosphate residues of DNA, stabilizing the specific conformation of the latter as well.[31] Çamur et al. have reported that indium (III) phthalocyanines strongly bind to blood plasma proteins such as bovine serum albumin (BSA). They have presented a spectroscopic investigation of the binding of the water-soluble quaternized ionic and zwitterionic gallium (III) and indium (III) Pc complexes to BSA.[32]

The synthesis of novel tetra aminopropylamid substituted phthalocyanines, which can stimulate new discussions about their biochemical role in the organism, is exhibited in this work. For the applications of micellar media, interaction with blood plasma proteins and drug delivery on the other hand might be targets for their betaine or sulfobetaine derivatives.

2. Results and discussion
2.1. Syntheses and characterization
As shown in the Scheme, the synthetic procedures started with the synthesis of a 2-hydroxyethyl-3-morpholin-propylcarbamate (**1**) by the reaction of 4-(3-aminopropyl) morpholine and ethylene carbonate in approximately 2 days at room temperature. The yield was 73% and the formation of **1** was confirmed by the combination of IR, NMR, elemental analysis, and MS spectroscopic data. The IR spectrum of compound **1** indicated that the aliphatic O–H peak, the N–H peak belonging to the amide group, and the carbonyl peaks of amide and COO groups are at 3439, 3324, 1693, and 1256 cm^{-1} respectively. The ^{1}H NMR spectrum of **1** indicated that the N–H proton attached to heteroatom at δ: 6.03 ppm (s, 1H), and O–H proton at δ: 4.54 ppm (s, 1H). The 8 peaks in the ^{13}C NMR spectrum, elemental analysis, and mass spectra results supported the proposed structure as well.

Compound **2** was obtained by aromatic substitution reaction of 2-hydroxyethyl -3-morpholinpropyl-carba-mate (**1**) and 4-nitrophthalonitrile using K_2CO_3 in DMSO with stirring at room temperature under argon atmosphere for 3 days. The pure product was achieved in crystalline form in 53.4% yield and its melting point was 146 °C. The formation of **2** was confirmed by the combination of spectroscopic data. In the FT-IR spectrum, the indicative peaks appeared at 3303 cm^{-1}, 2964–2772 cm^{-1}, and 2231 cm^{-1} attributed to amide group N–H vibration, aliphatic C–H vibrations, and C≡N vibration of nitrile groups, respectively.

The ^{1}H NMR spectrum of **2** indicated that the aromatic protons appeared at δ: 8.07, 7.49, and 7.30 ppm, the N–H proton of the amide group at δ: 7.79 ppm, and aliphatic protons of CH$_2$ groups between δ: 4.33 ppm and 1.60 ppm. In the ^{13}C NMR spectrum 9 carbons (6 for aromatic carbons, 2 for nitrile carbons, and 1 for carbonyl carbon) of the amine group appeared at 162.2–106.8 ppm and aliphatic carbon as 6 peaks at 68.4–26.4 ppm. The 7th aliphatic carbon of molecule **1** seen at 40.07 ppm should be identical for molecule **2** and it is under the intensive DMSO-d$_6$ peaks that appeared at 41.05–39.59 ppm. Consequently, all the peaks are

indicative and support the proposed structure. LCMS-MS (ESI$^+$) mass spectra of **2** indicated the molecular
ion peak at 359 m/z as [M+H]$^+$.
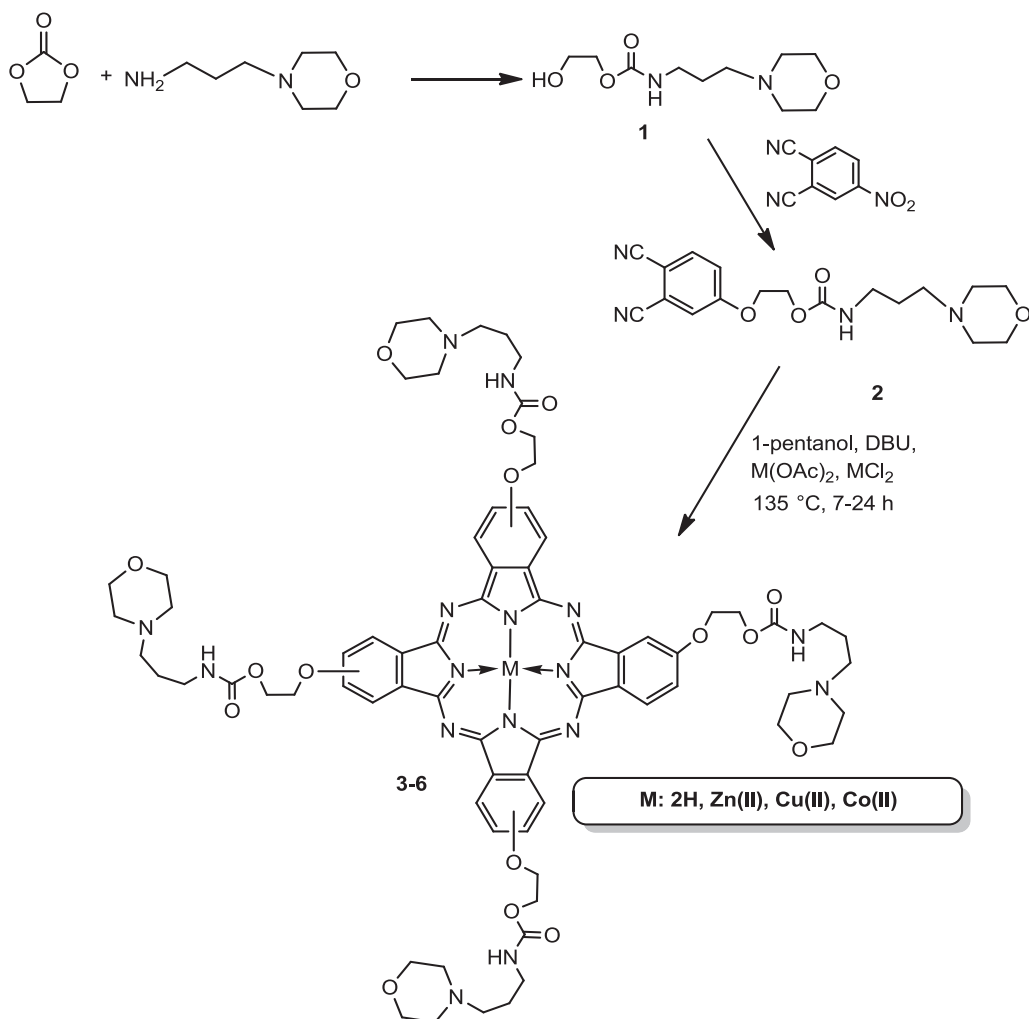
Scheme. Synthesis route for Pc complexes.

  2 and LiCl were refluxed in 1-pentanol at 135 °C for about 24 h to synthesize complex **3** (H$_2$Pc) by the
tetramerization of the phthalonitrile moiety. The preformed Li$_2$Pc was converted into H$_2$Pc by precipitating
with water. The sharp peak in the FT-IR spectrum for the C≡N vibration of phthalonitrile **2** at 2231 cm^{-1}
that disappeared during the conversion into phthalocyanine is indicative of H$_2$Pc formation. The characteristic
FT-IR band of the H$_2$Pc ring is an N–H stretch that appeared at 3295 cm^{-1}. Stretching of aromatic C–H and
aliphatic C–H was observed at 3070 cm^{-1} and 2949-2812 cm^{-1} respectively, as well. The ^{1}H NMR spectrum
of the prepared metal-free phthalocyanine (**3**) was recorded in DMSO-d$_6$ solution and the corresponding peaks
were observed as multiplets at 8.03–6.99 ppm for the aromatic proton of the phthalocyanine ring and amide NH
protons due to the geometric isomer formation. The total integration values of these protons for both groups
were determined as 16H. The other aliphatic protons belonging to substituted groups were observed at their
respective regions and supported the proposed structure. The inner protons of the H$_2$Pc ring were not observed
clearly below 0 ppm as indicated in the literature.

In the UV-VIS spectrum of H_2Pc (**3**), the conventional absorption bands were observed as Q and B bands at 704 nm, 672 nm, 643 nm, and 340 nm, respectively (Figure 1). LCMS-MS (ESI$^+$) mass spectra of **3** indicated the molecular ion peak at 1436 m/z as $[M+H]^+$.
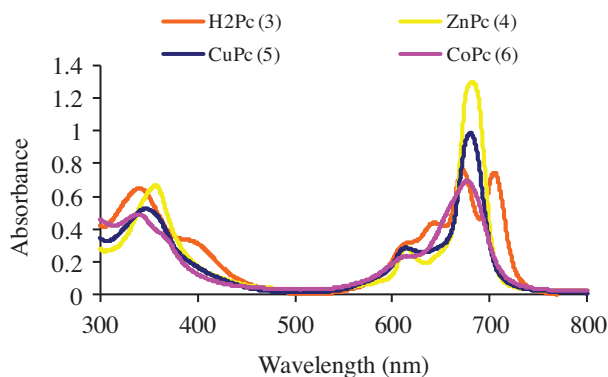
Figure 1. Absorption spectra of Pc complexes in DMSO (1×10^{-5} M).

Complexes **4**–**6** were synthesized by applying the same method described for complex **3** except the metal salts used and time: $ZnCl_2$, 7 h; $CuCl_2$, 7 h; and $Co(AcO)_2$, 7 h for **4**, **5**, and **6**, respectively. The formation of Pc complexes was confirmed by the combination of spectroscopic data. The FT-IR spectrum of the ZnPc (**4**), CuPc (**5**), and CoPc (**6**) obviously indicated the cyclotetramerization of the phthalonitrile derivative **2** with the disappearance of the C≡N peak at 2231 cm^{-1}.

The other indicative peaks for metallophthalocyanines such as stretching of the amide group, stretching of aromatic C–H, aliphatic C–H, and carbonyl C=O vibrations were observed in their respective regions. All the indicative peaks in the FT-IR spectrum supported the proposal structures. The ^{1}H NMR spectrum of **4** was recorded in DMSO d$_6$ and the obtained multiplets at aromatic and aliphatic regions for the corresponding protons accorded with the proposed structure. It can be predicted from the observed NMR results that ZnPc also was obtained as a mixture of isomers and the ^{13}C NMR results for **3** and **4** did not give illustrative information.

The UV-Vis spectra of the phthalocyanine complexes exhibit characteristic B and Q bands at around 300–400 nm and 600–700 nm, respectively (Figure 1). The ground state electronic spectra of the studied tetra-substituted metallophthalocyanines showed characteristic absorptions in the B band region at 356 nm for compound **4**, 353 nm for compound **5**, and 342 nm for compound **6** in DMSO. The absorptions of these complexes were also observed at 682 nm, 682 nm, and 680 nm as main Q bands, respectively.

In the mass spectrum of metallophthalocyanines, the presence of molecular ion peaks at m/z = 1498 $[M]^+$, 1497 $[M]^+$, and 1493 $[M]^+$ confirmed the proposed structures of ZnPc (**4**), CuPc (**5**), and CoPc (**6**), respectively. The elemental analysis results supported the proposal structures of **4**, **5**, and **6**.

2.2. Solubility and aggregation properties

The solubility behavior of the H_2Pc (**3**) and metallophthalocyanine complexes **4**, **5**, and **6** was investigated in DCM, THF, EtOH, MeOH, DMF, DMSO, and water, which were ordered from nonpolar to polar. The synthesized phthalocyanines showed good solubility in DMSO (Figure 1). The Lambert–Beer law was obeyed for compounds **3** and **4** at the studied concentration range (1×10^{-5}–1×10^{-6} M) as well.

Aggregation of phthalocyanines in solutions is dependent on the solvent, concentration, temperature, substituents linked to the main core, and complexed metal ion.[23] The aggregation behavior of the H_2Pc (**3**) and ZnPc (**4**) was investigated to characterize all the prepared complexes. The aggregation studies were performed in different solvents and concentrations in DMF. Figures 2a and 2b show example UV-Vis spectra of the mentioned Pcs **3** and **4** in different solvents, respectively. H_2Pc (**3**) and ZnPc (**4**) both exhibited the lowest aggregation in DMF. However, H_2Pc showed high aggregation in DCM and EtOH as judged by a blue shift of the Q band, and it was not soluble in methanol. ZnPc was soluble in MeOH and showed the highest aggregation when it was compared with the other solvents. In the UV-Vis spectra of the Pcs, B bands are not affected by the aggregation of the molecules and the absorption values increase regularly with the increase in concentrations. However, Q bands in the spectra, which are affected by concentration of the solutions and the aggregation properties on the dissolved molecules, do not rise diagonally with the increase in concentration as occurs in the B bands. There are some definitions in the literature as aggregation number[33,34] to determine the ratio of monomer concentration to the concentrations of other species such as dimers and trimers. To be able to obtain a mathematical value by the elimination of the concentrations to show the aggregation properties solely, the recorded maximum absorption values of these 2 bands can be divided. The ratio of these B and Q bands at maximum absorbance gives a value that can be named aggregation value. The aggregation value can be calculated from Eq. (1).

$$\mathcal{A}_v = A_{\mathcal{B}_{max}}/A_{Q\ max} \tag{1}$$

From Eq. (1), the calculated aggregation values of H_2Pc in various solvents were ordered as EtOH > DCM > THF > DMSO > DMF (Figure 3a). The calculated aggregation values of ZnPc (**4**) in different solvents gave the MeOH > EtOH > DCM > DMSO > THF > DMF order (Figure 3b).
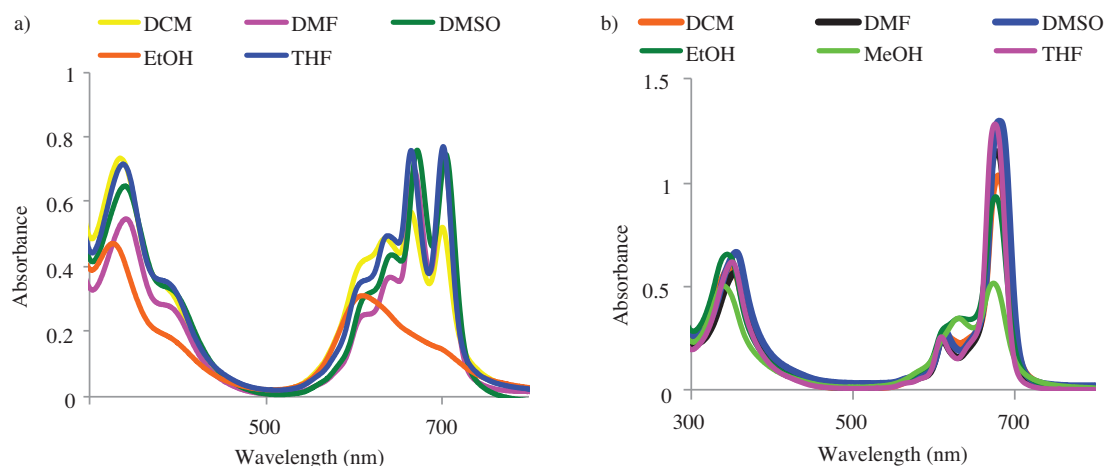

Figure 2. a) UV-Vis spectra of H_2Pc (**3**) in 5 different solvents, b) UV-Vis spectra of ZnPc (**4**) in 6 different solvents (concentrations = 1×10^{-5} M).

The aggregation and concentration relevancies of H_2Pc (**3**) and ZnPc (**4**) were studied in DMF due to having the lowest aggregation values ($\mathcal{A}_v$'s). They exhibited nonaggregated spectra in 1×10^{-5}–1×10^{-6} M range and almost constant $\mathcal{A}_v$'s as 0.75 and 0.49 respectively (Figures 4 and 5).
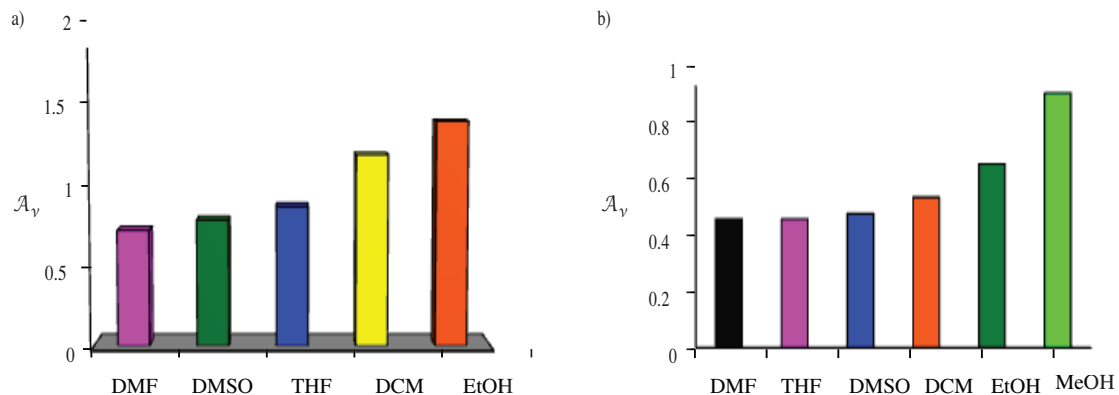
Figure 3. a) Aggregation values ($\mathcal{A}_v$) of H_2Pc (**3**) in DCM, DMF, DMSO, EtOH, and THF, b) Aggregation values ($\mathcal{A}_v$) of ZnPc (**4**) in DCM, DMF, DMSO, EtOH, MeOH, and THF (concentrations $= 1 \times 10^{-5}$ M).
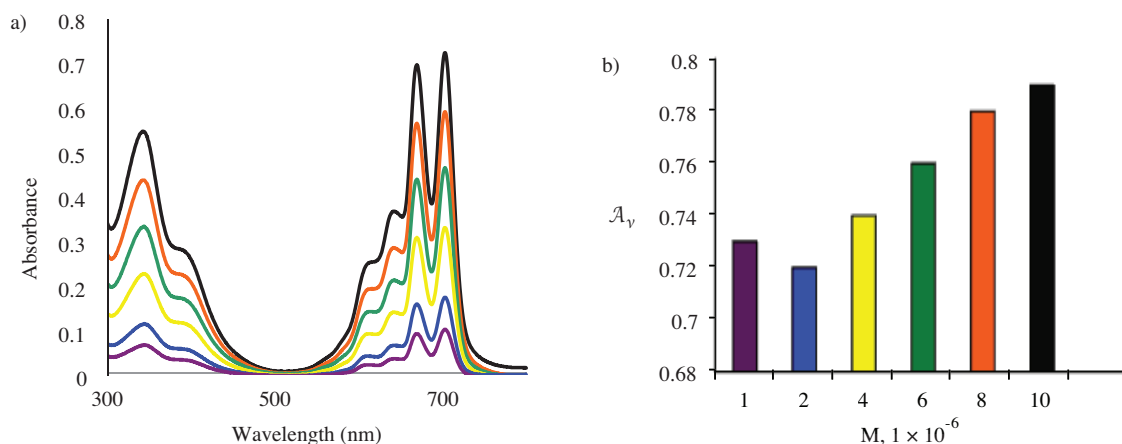

Figure 4. a) Aggregation behavior of H_2Pc (**3**) in DMF at different concentrations, b) Aggregation values ($\mathcal{A}_v$) of H_2Pc (**3**) in DMF at different concentrations: 10×10^{-6}, 8×10^{-6}, 6×10^{-6}, 4×10^{-6}, 2×10^{-6}, 1×10^{-6} M.
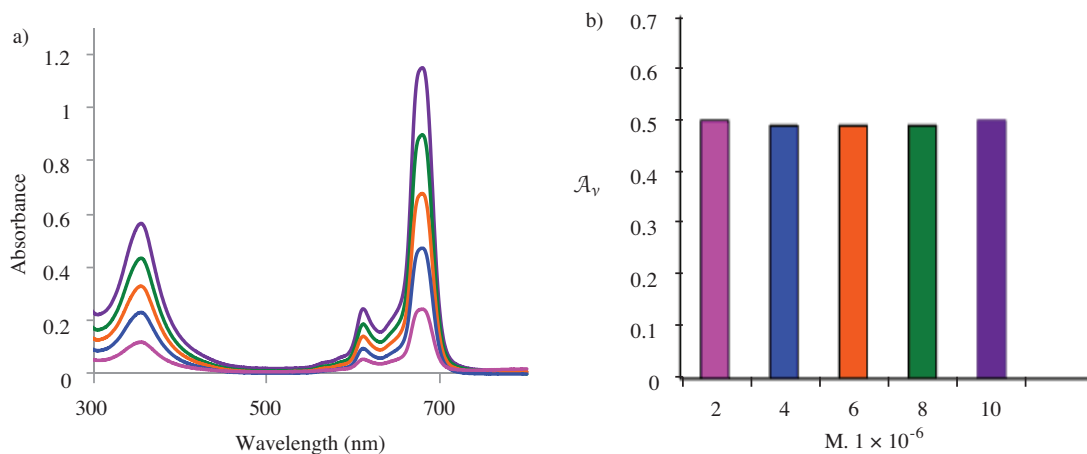

Figure 5. a) Aggregation behavior of ZnPc (**4**) in DMF at different concentrations, b) Aggregation values ($\mathcal{A}_v$) of ZnPc (**4**) in DMF at different concentrations: 10×10^{-6}, 8×10^{-6}, 6×10^{-6}, 4×10^{-6}, 2×10^{-6} M.

2.3. Solubility in water

The solubility of H_2Pc and ZnPc in water was examined in their critical solutions, which characterized their maximum aggregated situation before the precipitation. The critical solutions of H_2Pc and ZnPc were prepared as 10 mL, 1×10^{-4} M by dissolving DMSO (2 mL) and adding water. Then the stock solution was diluted to 1×10^{-6} M by adding a solvent mixture of DMSO/water (1/4). DMSO was chosen as one of the good solvents to satisfy the desired critical solution. Moreover, 1×10^{-2} M HCl solution was added in 10-μL intervals to 10 mL of the H_2Pc and ZnPc solutions to fulfill equal mol ratio of the substituted tertiary amines. They showed a blue-shifted band at 604 nm for H_2Pc and 634 nm for ZnPc because of aggregation (Figures 6a and 6b) and insufficient solubility increments in water via quaternization of the tertiary amine substituents (Figures 7a and 7b).
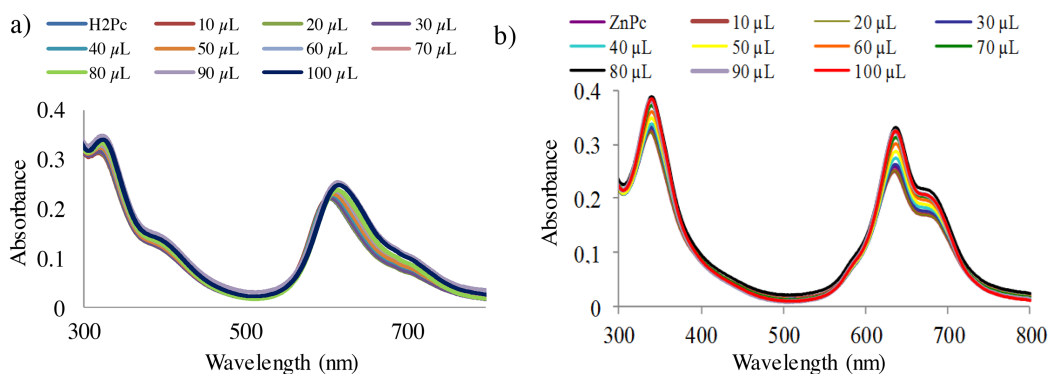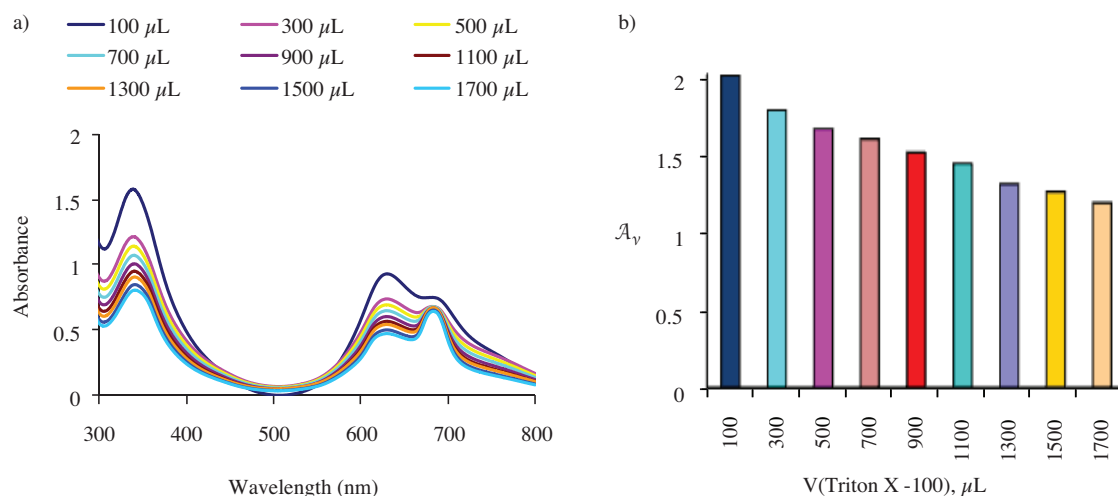

Figure 6. a) Changes in the UV-Vis spectra of H_2Pc in DMSO/water solution (1.0×10^{-6} M) by the addition of 1×10^{-2} M HCl (10-μL intervals), b) Changes in the UV-Vis spectra of ZnPc solution in DMSO/water (1.0×10^{-6} M) by the addition of 1×10^{-2} M HCl (10-μL intervals).
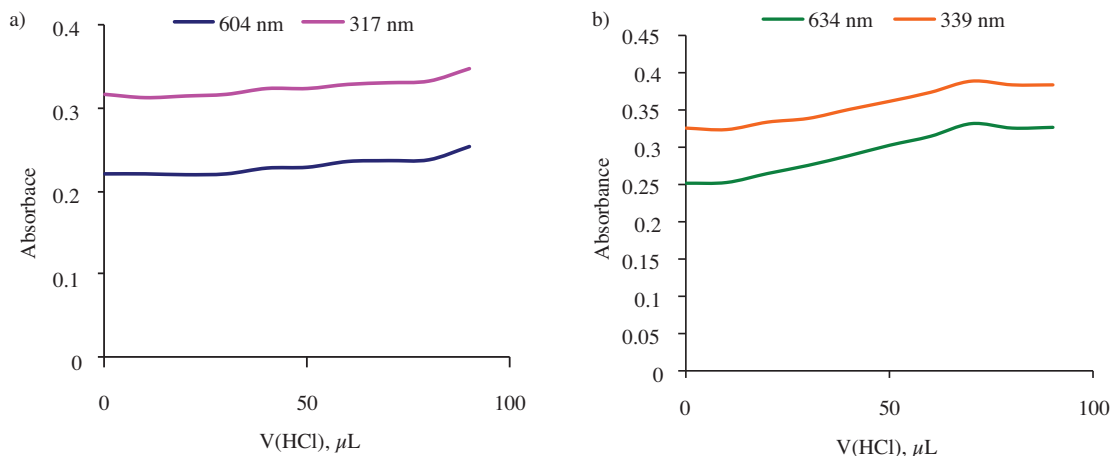

Figure 7. a) Absorption changes in Q band (604 nm) and B band (317 nm) of H_2Pc, b) Absorption changes in Q band (634 nm) and B band (339 nm) of ZnPc.

The solubility study of ZnPc in the DMSO/water critical solution (1×10^{-5} M) system was examined by adding pH 4.55 and pH 3.61 HCl solutions (100 μL) and Triton X-100 solution in water (1×10^{-3} M,

100-μL intervals) as ionizing agent and surfactant solution to reduce the aggregation tendency, respectively. Adding Triton X-100 as a surfactant also increased the solubility and broke up the aggregation (Figure 8). The use of HCl solution with pH 4.55 increased both the ionic strength of the solution and the aggregation behavior, and the solubility of ZnPc was decreased (Figure 9). When the collected $\mathcal{A}_v$ data of ZnPc solution treated with HCl solution (pH 4.55) and without HCl solution in the presence of Triton X-100 were compared, very similar changes were observed (Figures 8 and 9). However, the water solubility of ZnPc increased with the addition of HCl via quaternizing of the bearing tertiary amines groups on the substituents when the pH 3.61 HCl solution was used (Figure 10).

Figure 8. a) Changes in the UV-Vis spectra of ZnPc (1.0×10^{-5} M) in DMSO/water by the addition of 1×10^{-3} M Triton X-100, 100-μL intervals, b) Changes in the aggregation values ($\mathcal{A}_v$) of ZnPc.
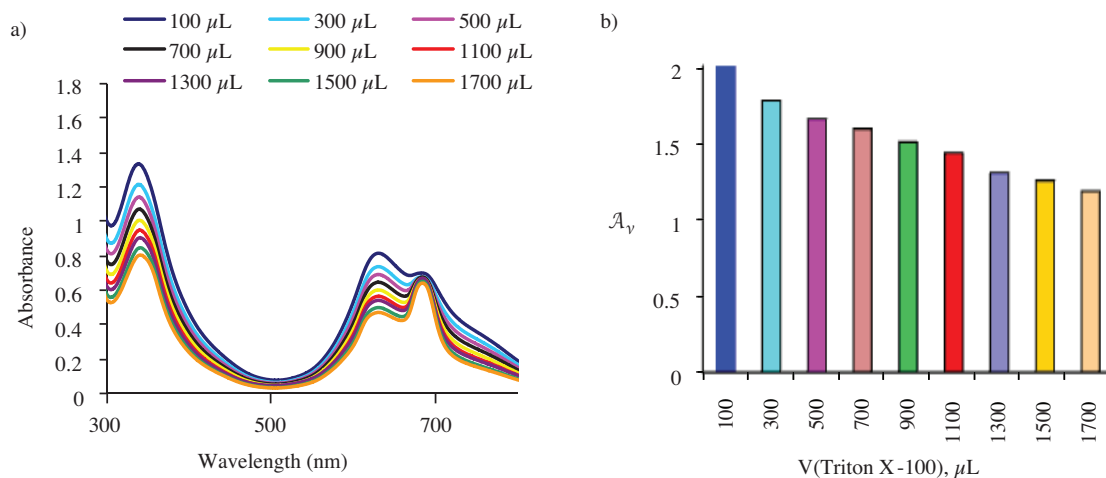
Figure 9. a) Changes in the UV-Vis spectra of acidified ZnPc solution (1.0×10^{-5} M) in DMSO/water (by the addition of HCl solution having pH 4.45, at one time) during the addition of 1×10^{-3} M Triton X-100 solution, 100-μL intervals, b) Changes in the aggregation values ($\mathcal{A}_v$) of ZnPc.
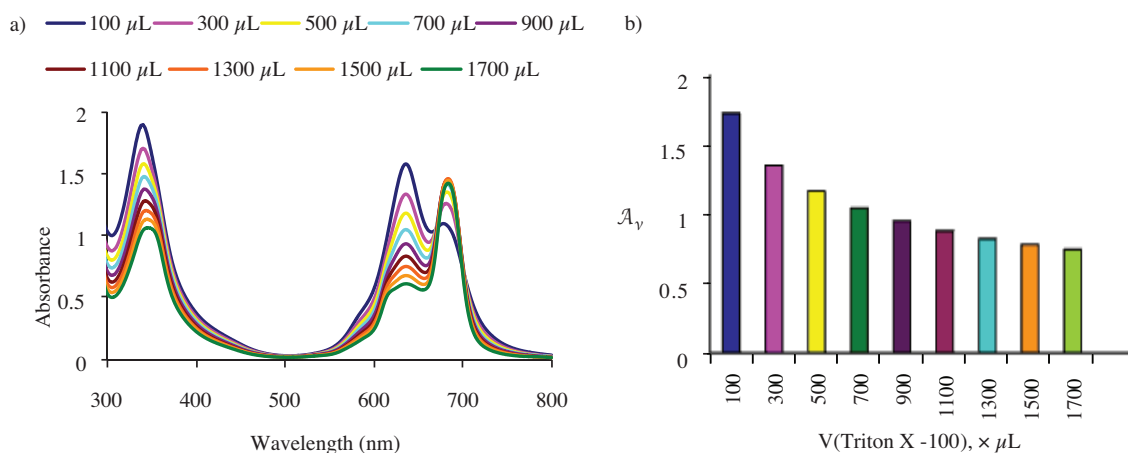
Figure 10. a) Changes in the UV-Vis spectra of acidified ZnPc solution (1.0×10^{-5} M) in DMSO/water (by the addition of HCl solution having pH 3.61, at one time) during the addition of 1×10^{-3} M Triton X-100 solution, 100-μL intervals, b) Changes in the aggregation values ($\mathcal{A}_v$) of ZnPc.

In conclusion, tetra aminopropylamid substituted phthalocyanines were synthesized as soluble nonionic modified species and characterized by UV-Vis, FT-IR, and mass spectroscopies. The effects of solvent (DMF, DMSO, THF, EtOH) and concentration (in DMF) on the aggregation properties of these tetra aminopropylamid substituted phthalocyanines (H_2Pc, ZnPc) were investigated. Aggregation value ($\mathcal{A}_v$) has been described as the function of ratio of B to Q bands. From the $\mathcal{A}_v$ results aggregation tendencies can be ordered as EtOH > DCM > THF > DMSO > DMF for H_2Pc and MeOH > EtOH > DCM > DMSO > THF > DMF for ZnPc.

3. Experimental

3.1. Materials and characterization techniques

All reagents and solvents obtained from commercial suppliers were reagent grade quality. Dimethyl sulfoxide (DMSO), N,N-dimethylformamide (DMF), dichloromethane (DCM), chloroform ($CHCl_3$), tetrahydrofuran (THF), methanol (MeOH), ethanol (EtOH), 1-pentanol, n-hexane, and acetonitrile were purchased from Merck; 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), potassium carbonate (K_2CO_3), lithium chloride, zinc chloride, copper chloride, and cobalt acetate were purchased from Aldrich. Solvents were dried via an A3 molecular sieve and stored in the presence of it. 4-Nitro phthalonitrile was prepared according to the literature procedure.[35] All reactions were carried out under argon atmosphere, using the standard Schlenk technique. Thin-layer chromatography (TLC) was performed using silica gel 60 HF$_{254}$ as an adsorbent. Melting point (mp) was determined using a Barnstead-Electrothermal 9200 apparatus. Electronic spectra were recorded on a Shimadzu UV-2600 spectrophotometer using a 1-cm quartz cell. Infrared spectra were recorded on a PerkinElmer Spectrum-Two FT-IR (ATR sampling accessory) spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded as CDCl$_3$ and DMSO-d$_6$ solutions on a Varian Mercury Plus 300 MHz spectrometer. Mass analyses were measured on a Micro-Mass Quatro LC/ULTIMA LC–MS/MS spectrometer. pH measurements were recorded on a PHM210 Standard pH meter calibrated up with 3 standards for 4, 7, and 10 values. The elemental analyses were performed on a LECO CHNS-932 instrument at Middle East Technical University.

3.2. Synthesis

3.2.1. 2-Hydroxyethyl -3-morpholinpropylcarbamate (1)

4-(3-Aminopropyl)morpholine (0.82 g, 5.7 mmol) was added to melted ethylene carbonate (0.5 g, 5.6 mmol) drop-wise over approximately 40 min at 45 °C. The reaction mixture was stirred at room temperature for 48 h. The residue was dissolved in dichloromethane (40 mL), the organic phase was washed with brine solution (2 × 20 mL), and the solvent was evaporated to dryness. The residue was dried under vacuum at 40 °C on a sonication bath for 3 h and the pure product was obtained as light yellow viscose liquid. Yield: 0.97 g, (73%). Anal. Calc. for $C_{10}H_{20}N_2O_4.H_2O$ (250 g/mol) (%): C, 47.99; H, 8.86; N, 11.19. Found (%): C, 47.27; H, 8.49; N, 11.01. IR, V_{max} (cm^{-1}): 3439 (O–H), 3324 (N–H), 3074 (Ar–H), 2948–2815 (C–H), 1693 (C=O), 1533–1360 (C–C), 1256 (COO), 1114–1033 (C–O), 862, 631. ^{1}H NMR (CDCl$_3$), (δ: ppm): 6.03 (s, 1H, NH), 4.54 (s, 1H, OH), 4.17 (t, J = 4.4 Hz 2H, CH$_2$), 3.76 (t, J = 4.5 Hz 2H, CH$_2$), 3.71 (t, J = 4.6 Hz 4H, CH$_2$), 3.24 (m, 2H, CH$_2$), 2.44–2.39 (m, 6H, CH$_2$), 1.69 (m, 2H, CH$_2$). ^{13}C NMR (CDCl$_3$), (δ: ppm): 157.2, 66.9, 64.8, 61.3, 56.0, 53.7, 40.0, 26.0. LCMS-MS (ESI$^+$), (m/z): 233 [M+H]$^+$.

3.2.2. 4-(2-Ethoxy-3-morpholinpropylcabamate)phthalonitrile (2)

A mixture of 2-hydroxyethyl-3-morpholinpropylcarbamate (**1**) (0.26 g, 1.1 mmol), 4-nitrophtalonitrile (0.19 g, 1.1 mmol), and K$_2$CO$_3$ (0.5 g, 3.6 mmol) in dry dimethyl sulfoxide (DMSO, 5 mL) was stirred at room temperature. Further anhydrous K$_2$CO$_3$ (2 × 0.5 g, 7.2 mmol) were added to reaction mixture at 12-h intervals. The suspension was stirred at room temperature for 3 days under argon atmosphere. The reaction was monitored by TLC using THF/hexane (3/4) as a mobile phase on silica-gel plates. The green-brown reaction mixture was poured into an ice–water mixture (100 mL) and precipitated. The crude product was isolated by vacuum filtration and the precipitate was dissolved in hot ethanol (15 mL) to remove unwanted side products. The solution was filtrated off and evaporated to dryness. The pure product was obtained by recrystallization from acetonitrile. Yield: 0.26 g, (53.4%). mp: 146 °C. Anal. Calc. for $C_{18}H_{22\ 4}O_4.H_2O$ (376 g/mol) (%): C, 57.44; H, 6.43; N, 14.88. Found (%): C, 57.09; H, 6.23; N, 14.65. IR, V_{max} (cm^{-1}): 3303 (N–H) 3085–3037 (Ar, C–H), 2964–2772 (Aliph., C-H), 2231 (C≡N), 1689 (C=O), 1597–1560 (C=C), 1464–1408 (C–C), 1253 (COO), 1133 (C–O), 964, 837. ^{1}H NMR (DMSO-d$_6$), (δ: ppm): 8.07 (d, J = 11.8 Hz 1H, Ar–H), 7.79 (s, 1H, NH), 7.49 (d, J = 2.5 Hz 1H, Ar–H), 7.30 (s, 1H, Ar–H), 4.33 (m, 4H, O–CH$_2$), 3.54 (t, J = 4.6 Hz 4H, CH$_2$) 3.00 (m, 2H, CH$_2$), 2.51–2.21 (m, 6H, CH$_2$) and 1.60 (m, 2H, CH$_2$). ^{13}C NMR (DMSO-d$_6$), (δ: ppm): 162.2, 156.5, 136.4, 120.9, 120.6, 117.0, 116.8, 116.3, 106.8, 68.4, 66.8, 62.4, 56.3, 53.9, 26.4. LCMS-MS (ESI$^+$), (m/z): 375 [M.H$_2$O–H], 359 [M+H]$^+$.

3.2.3. 2(3),9(10),16(17),23(24)-Tetrakis-[2-ethoxy-3-morpholinpropylcabamate] phthalocyanine (3)

A mixture of **2** (0.30 g, 0.8 mmol), anhydrous lithium chloride (0.17 g, 0.4 mmol), and DBU (0.11 mL, 0.75 mmol) in 1-pentanol (6 mL) was stirred at 135 °C for 24 h under argon atmosphere. After completion of the reaction, the mixture was precipitated with water (15 mL) and the crude product was collected by centrifuge. The green product was purified by dissolving in methanol and re-precipitating several times with a MeOH/water (1/1) mixture. The green solid product was washed successively with n-hexane, acetonitrile, diethyl ether, and water, and then dried under vacuum over P$_2$O$_5$. Yield: 0.126 g, (40.2%). Anal. Calc. $C_{72}H_{90}N_{16}O_{16}$ (1435 g/mol) (%): C, 60.24; H, 6.32; N, 15.61. Found (%): C, 60.02; H, 6.12; N, 15.20. IR, V_{max} (cm^{-1}): 3295

(N–H), 3070 (Ar–CH), 2949–2812 (Aliph. C–H), 1695 (C=O), 1611–1525 (C=C), 1481–1341 (C–C), 1233, 1113, and 824. ^{1}H NMR (DMSO-d$_6$), (δ: ppm): 8.03–6.99 (m, 16H, Ar–H and CONH), 4.43 (m, 16H, O–CH$_2$), 3.64 (m, 16H, CH$_2$) 3.08 (m, 8H, CH$_2$), 2.54–2.25 (m, 24H, CH$_2$) and 1.68 (m, 8H, CH$_2$). UV/vis (DMSO): λ_{max}. (log ε) 704 (4.31), 672 (4.33), 643 (4.08), 340 (4.17). LCMS-MS (ESI$^+$), (m/z): 1436 [M+H]$^+$.

3.2.4. 2(3),9(10),16(17),23(24)-Tetrakis-[2-ethoxy-3-morpholinpropylcabamate] phthalocyaninato zinc(II) (4)

A mixture of **2** (0.300 g, 0.8 mmol), anhydrous zinc (II) chloride (0.028 g, 0.2 mmol), and DBU (0.11 mL, 0.75 mmol) in 1-pentanol (6 mL) was heated to 135 °C and stirred for 7 h under argon atmosphere. After cooling to room temperature, the dark green reaction mixture was precipitated by dropping into a MeOH/water (1/1) mixture (30 mL). The crude product was collected by centrifuge, washed with the same solvent system several times, and dried under vacuum at ambient temperature. Unreacted organic matter and residual 1-pentanol were removed from the product by Soxhlet extraction with acetonitrile (80 mL) for 48 h. The green product was recovered by dissolving with MeOH (15 mL), re-precipitating with water, and collecting by centrifuging. The pure product was washed with diethylether and n-hexane and dried under vacuum over P$_2$O$_5$. The green product showed excellent solubility in MeOH, EtOH, THF, and DMSO. Yield: 0.141 g, (44.9%). Anal. Calc. C$_{72}$H$_{88}$N$_{16}$O$_{16}$Zn (1498 g/mol) (%): C, 57.69; H, 5.92; N, 14.95. Found (%): C, 57.99, H, 6.04, N, 14.30. IR, V_{max} (cm^{-1}): 3310 (N–H), 3067 (Ar–CH), 2948–2812 (C–H), 1698 (C=O), 1606–1530 (C=C), 1487–1333 (C–C), 1226, 1113, 1088, 1041, and 955. ^{1}H NMR (DMSO-d$_6$), (δ: ppm): 8.05–7.01 (m, 16H, Ar–H and CONH), 4.45 (m, 16H, O–CH$_2$), 3.62 (m, 16H, CH$_2$) 3.06 (m, 8H, CH$_2$), 2.55–2.28 (m, 24H, CH$_2$) and 1.71 (m, 8H, CH$_2$). UV/vis (DMSO): λ_{max}. (log ε) 682 (4.86), 614 (4.02), 356 (4.19). LCMS-MS (ESI$^+$), (m/z) : 1498 [M]$^+$.

3.2.5. 2(3),9(10),16(17),23(24)-Tetrakis-[2-ethoxy-3-morpholinpropylcabamate] phthalocyaninato-copper(II) (5)

A mixture of **2** (0.06 g, 0.17 mmol), anhydrous copper (II) chloride (0.005 g, 0.04 mmol), and DBU (0.02 mL, 0.19 mmol) in 1-pentanol (2 mL) was stirred at 135 °C for 7 h under argon atmosphere. After completion of the reaction the mixture was precipitated with a MeOH/water (1/1) (15 mL) mixture and collected by centrifuging. The crude product was purified in the same way as for compound **4** and dried under vacuum over P$_2$O$_5$. The green Pc showed excellent solubility in chloroform, THF, and DMSO. Yield: 0.023 g, (36.5%). Anal. Calc. C$_{72}$H$_{88}$N$_{16}$O$_{16}$Cu (1497 g/mol) (%): C, 57.76; H, 5.92; N, 14.97. Found (%): C, 57.24; H, 5.47; N, 14.61. IR, V_{max} (cm^{-1}): 3326 (N–H), 3063 (Ar–CH), 2949–2810 (C–H), 1690 (C=O), 1608–1587 (C=C), 1484–1343 (C–C), 1227, 1115, 1092, 1047, and 959. UV/vis (DMSO): λ_{max}. (log ε) 682 (4.57), 616 (4.11), 353 (4.23). LCMS-MS (ESI$^+$), (m/z): 1497 [M]$^+$.

3.2.6. 2(3), 9(10), 16(17), 23(24)-Tetrakis-[2-ethoxy-3-morpholinpropylcabamate] phthalocyaninato cobalt (II) (6)

A mixture of **2** (0.09 g, 0.25 mmol) and anhydrous cobalt (II) acetate (0.012 g, 0.07 mmol) in 1-pentanol (2 mL) and DBU (0.02 mL, 0.19 mmol) was stirred at 135 °C under argon atmosphere for 7 h. The mixture was poured into water after cooling to room temperature and the product was extracted with ethyl acetate (2 × 20

mL). Ethyl acetate was evaporated to dryness. The blue crude product washed with cold MeOH and dissolved in hot ethanol (15 mL). The solution was filtrated off and evaporated to dryness. The blue solid product was washed several times with water, n-hexane, and acetonitrile and dried under vacuum over P_2O_5. Yield: 0.042 g, (44.7%). Anal. Calc. $C_{72}H_{88}N_{16}O_{16}Co$ (1493 g/mol) (%): C, 57.94; H, 5.94; N, 15.02. Found (%): C, 57.09; H, 5.12; N, 14.78. IR, V_{max} (cm^{-1}): 3292 (N–H), 3067 (Ar–CH), 2930–2816 (Aliph. C–H), 1712 (C=O), 1608–1522 (C=C), 1485–1343 (C–C), 1233, 1063, 962, and 820. UV/vis (DMSO): λ_{max}. (log ε) 680 (4.30), 618 (4.15), 342 (4.22). LCMS-MS (ESI$^+$), (m/z): 1493 [M]$^+$.

3.3. Examination of solubility and aggregation values

Molecular solubility and aggregation values of the prepared phthalocyanines (**3**, **4**) were examined by UV-vis spectrophotometric measurements on the 1×10^{-5} M solutions in organic solvents. Stock solutions of phthalocyanines were prepared in the related organic solvents (DCM, THF, EtOH, MeOH, DMF, and DMSO) from nonpolar to polar as 1×10^{-4} M, 25 mL, and then diluted to 1×10^{-5} M concentrations. To characterize the pH effect on the solubility in water for **3** and **4**, solutions were prepared by dissolving **3** and **4** in 2 mL of DMSO and adding 8 mL of water (1×10^{-4} M). The stock solution was diluted to 1×10^{-6} M by adding the same amount of DMSO and water. HCl solution (1×10^{-2} M) in water as 10-μL volumes was added to 1 $\times 10^{-5}$ M solutions 9 times. Moreover, **4** was examined by adding 2 different HCl solutions (10 μL with pH 4.55 and 3.61 values) and Triton X-100 solution in water (1×10^{-3} M, 100-μL intervals) to characterize the pH and surfactant effects on the solubility in water.

Acknowledgment

References

1. Leznoff, C. C.; Lever, A. B. P. *Phthalocyanines Properties and Applications;* Wiley, VCH: New York NY, USA, 1989–1996.

2. Zugle, R.; Nyokong, T. *J. Mol. Catal. A.* **2012**, *358*, 49–57.

3. Ma, L.; Zhang, Y.; Ma, P. Y. L.; Zhang, Y.; Yuan, P. *Opt. Express.* **2010**, *18*, 17666–17971.

4. Yuksel, F.; Durmus, M.; Ahsen, V. *Dyes Pigments* **2011**, *90*, 191–200.

5. Lee, W.; Yuk, S. B.; Choi, J.; Jung, D. H.; Choi, S. H.; Park, J.; Kim, J. P. *Dyes Pigments* **2012**, *92*, 942–948.

6. Hu, X.; Xia, D.; Zhang, L.; Zhang, J. *J. Power Sources* **2013**, *231*, 91–96.

7. Nyokong, T.; Antunes, E. *Coord. Chem. Rev.* **2013**, *257*, 2401–2418.

8. Yildiz, S. Z.; Colak, S.; Tuna, M. *J. Mol. Liq.* **2014**, *195*, 22–29.

9. Chowdhury, A.; Biswas, B.; Majumder, M.; Sanyal, M. K.; Mallik, B. *Thin Solid Films* **2012**, *520*, 6695–6704.

10. Giribabu, L.; Singh, V. K.; Jella, T.; Soujanya, Y.; Amat, A.; Angelis, F. D.; Yella, A.; Gao, P.; Nazeeruddin, M. K. *Dyes Pigments* **2013**, *98*, 518–529.

11. Jiang, Z.; Shao, J.; Yang, T.; Wang, J.; Jia, L. *J. Pharmaceut. Biomed.* **2014**, *87*, 98–104.

12. Zheng, B. Y.; Zhang H. P.; Ke, M. R.; Huang, J. D. *Dyes Pigments* **2013**, *99*, 185–191.

13. Ün, İ.; Zorlu, Y.; İbişoğlu, H.; Dumoulin, F.; Ahsen, V. *Turk. J. Chem.* **2013**, *37*, 394–404.

14. Nemykin, V. N.; Hadt, R. G.; Belosludov, R. V.; Mizuseki, H.; Kawazoe, Y. *J. Phys. Chem. A.* **2007**, *111*, 12901–12913.

15. Sevim, A. M.; Arıkan, S.; Özçeşmeci, I.; Gül, A. *Synthetic Met.* **2013**, *183*, 1–7.

16. Karaoğlan, G. K.; Gümrükçü, G.; Koca A.; Gül, A.; Avcıata, U. *Dyes Pigments* **2011**, *90*, 11–20.

17. Göksel, M.; Durmus, M.; Atilla, D. *J. Photoch. Photobio. A.* **2013**, *266*, 37–46.

18. Fashina, A.; Antunes, E.; Nyokong, T. *J. Mol. Struct.* **2014**, *1068*, 245–254.

19. Ahmed I.; Moradi-Araghi, A.; Patel, B. B.; Stewart, *W. S. United States Patent 5922653*, Jul. **1999**.

20. Bergamini, P.; Marvelli, L.; Marchi, A.; Bertolasi, V.; Fogagnolo, M.; Formaglio, P.; Sforza, F. *Inorg. Chim. Acta.* **2013**, *398*, 11–18.

21. Lee, H. H.; Wilson, W. R.; Ferry, D. M.; Zijl, P. V.; Pullen, S. M.; Denny, W. A. *J. Med. Chem.* **1996**, *39*, 2508–2517.

22. Rong, D.; Phillips, V. A.; Rubio, R. S.; Castro, M. Á.; Wheelhouse, R. T. *Tetrahedron Lett.* **2008**, *49*, 6933–6935.

23. Buston, J. E. H.; Coldham, I.; Mulholland. K. R. *Tetrahedron: Asymmetr.* **1998**, *9*, 1995–2009.

24. Bıyıklıoğlu, Z. *Synthetic Met.* **2012**, *162*, 26–34.

25. Brault, N. D.; White, A. D.; Taylor, A. D.; Yu, Q.; Jiang, S. *Anal. Chem.* **2013**, *85*, 1447–1453.

26. Santisa, S. D., Diociaiutic, M.; Cametti, C.; Masci, G. *Carbohyd. Polym.* **2014**, *101*, 96–103.

27. Kim, G.; Yoo, C. E.; Kim, M.; Kang, H. J.; Park, D.; Lee, M.; Huh, N. *Bioconjugate Chem.* **2012**, *23*, 2114 − 2120.

28. BI O'Lenick, Jr. et al. *United States Patent 6620794*, Sep. **2003**.

29. Dahlmann et al. *United States Patent 2004/016330,* Aug. **2004**.

30. Chibale, K.; Chipeleme, A.; Warren, S. *Tetrahedron Lett.* **2002**, *43*, 1587–1589.

31. Kalisiak, J.; Trauger, S. A.; Kalisiak, E.; Morita, H.; Fokin, V. V.; Adams, M. W. W.; Sharpless, K. B.; Siuzdak, G. *J. Am. Chem. Soc.* **2009**, *131*, 378–386.

32. Çamur, M.; Ahsen, V.; Durmus, M. *J. Photoch. Photobio. A.* **2011**, *219*, 217–227.

33. Camp, P. J.; Jones, A. C.; Neely, R. K.; Speirs, N. M. *J. Phys. Chem. A* **2002**, *106,* 10725-10732.

34. Doane, T.; Chomas, A.; Srinivasan, S.; Burda, C. *Chem. Eur. J.* **2014**, *20*, 8030–8039.

35. Young, J. G.; Onyebuagu, W. *J. Org. Chem.* **1990**, *55*, 2155–2159.