Microwave-Assisted Synthesis, Characterization and Aggregation Properties of Novel Metallophthalocyanines containing 2-aminothiophenol moieties

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Summary: The microwave-assisted synthesis and characterization of novel peripherally 2-aminothiophenol substituted metallophthalocyanines (M: Ni(II), Zn(II)) have been reported for the first time in this study. All the new compounds were characterized by a combination of FT-IR, ^{1}H-NMR, ^{13}C-NMR, and UV/vis spectroscopy techniques. The crystal structure of compound **(1)** was also determined by the single crystal diffraction technique. Aggregation properties of metallophthalocyanines were investigated at different concentrations in DMSO.

Keywords: Phthalocyanine, 2-aminothiophenol, X-Ray diffraction, Aggregation.

Introduction

The phthalocyanines are synthetic tetrapyrrolic macrocylic compounds which are not natural [1]. Phthalocyanines are very important industrial pigments that provide stable and strongly chromatic blue and green colors. Phthalocyanines have improved photophysical and photochemical properties due to strong absorbance at long wavelengths [2]. Phthalocyanines have overrun porphyrins in a number of applications because of their superior stability, improved spectroscopic characteristics, different coordination capability and architectural flexibility [3]. Phthalocyanines have found high-tech imaging technology like photoconducting agents in laser printers [4]. In addition, their novelty is rapidly growing in other fields where they are used as liquid crystals, chemical sensors, semiconductors, functional polymers and molecular metals, among others [5]. They have also been used as photosensitizer material in photodynamic therapy (PDT) [6, 7]. Absorption in the near-infrared (NIR) region that one of the requirements for a good photosensitizer [8]. Substitution of the ring with sulfur-containing groups results in a large red-shift of the Q-band, due to the electron-donating ability of these groups [9].

Although there are several reports about octa aminothiophenol substituted phthalocyanines at literature [10, 11] phthalocyanines containing tetra aminothiophenol moiety are not known. This work aims at microwave-assisted synthesis of novel tetra thiol substituted metallophtalocyanines and investigation of spectral and aggregation properties to determine suitable for the medical applications like photodynamic therapy.

Experimental

Materials and Methods

4-Nitro–1,2-dicyanobenzene was prepared according to the literature procedure [12]. 2-aminothiophenol was purchased from Merck Chemical Company. FTIR spectra were recorded by Perkin-Elmer Spectrum 100 Infrared Spectrometer. UV/vis spectra were recorded by Perkin-Elmer UV/vis spectrometer. ^{1}H-NMR and ^{13}C-NMR studies were performed by Agilent 400 FT-NMR. Elemental analyses were performed by the Instrumental Analyses Laboratory of TÜBİTAK Gebze Research Center. Microwave-assisted syntheses were carried out by using monomode Anton Paar microwave apparatus.

Preparation

4[(2-aminophenyl)thio]1,2-dicyanobenzene **(1)**

2-Aminothiophenol (0.72 g, 5.78 mmol) and 4-nitro 1,2-dicyanobenzene (1 g, 5.78 mmol) was dissolved in dry dimethylsulfoxide (5 ml). After stirring for 15 minutes, newly ground anhydrous K_2CO_3 (1.87 g, 11.56 mmol) was added to this solution. The reaction flask was heated under microwave irradiation at 150 ^{o}C for 10 min, with stirring and air-jet cooling. After reaction completed, the mixture was filtered and poured into ice. The formed solid material was filtered off and the crude product was purified by recrystallization from dry ethanol. Yield: 1,23 g (82%); m.p. 162-163^{o}C. Single crystals were obtained by slow evaporation from ethanol. FTIRν_{max}/cm^{-1}. 3460 (NH), 3359 (NH), 3104, 3081, 3039, 2231 (CN), 1602, 1573, 1511, 1475, 1446,

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1305, 1251, 766, 747. ^{1}H-NMR (DMSO-d$_6$) δ, ppm: 7.97-7.95(1H, d, ArCH), 7.716-7.711 (1H, d, ArCH), 7.35-7.32 (1H, d.d, ArCH) 7.30-7.25 (2H, m, ArCH), 6.89-6.87(1H, d.d, ArCH), 6.67-6.63 (1H, t.d, ArCH), 5.81 (2H, s, NH). ^{13}C-NMR (DMSO-d$_6$) δ, ppm: 151.25, 146.91, 137.61, 134.44, 132.86, 130.34, 129.83, 117.41, 116.50, 116.00, 115.81, 115.35, 110.31, 108.03. Anal. Calcd. For $C_{14}H_9N_3S$: C, 66.91; H, 3.61; N, 16.72 Found: C, 66.80; H, 3.58; N, 16.60.

Microwave-assisted synthesis of metallophthalocyanines **(1a and 1b)**

The general procedure was employed for the synthesis of various metallophthalocyanines (M: Ni, Zn) were described as follows.

Compound **(1)** (310 mg, 1.23 mmol), metal salt for corresponding metallophthalocyanine ($NiCl_2$, $Zn(CH_3COO)_2$, 0,29 mmol), n-hexanol (3 mL) and 2-3 drops of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) were charged together into a round-bottomed flask. The reaction flask was irradiated by a microwave apparatus at 180 °C for 20 min. After cooling to room temperature, formed solid product was filtered off and washed with ethanol. The obtained green product was purified by column chromatography (silica gel, EtOH-$CHCl_3$, 1:10). All synthesized phthalocyanines are soluble in $CHCl_3$ and DMSO.

Yield, melting point, elemental analysis, FT-IR and UV/vis spectra of the products were as follows.

Nickel phthalocyanine **(1a)**; Yield 270 mg (88%) m.p.> 200 °C. 3454 (NH), 3356 (NH), 3050, 1601, 1530, 1476, 1427, 1290, 1199, 1090, 728, 719. ^{1}H-NMR (DMSO-d$_6$) δ, ppm: 7.46-6.76 (28H, m, ArCH), 5.45 (8H, s, NH). Anal. Calcd. For $C_{56}H_{36}N_{12}S_4Ni$: C, 63.22; H, 3.41; N, 15.80 Found: C, 63.19; H, 3.25; N, 15.55. UV/vis (DMSO): λ_{max} /nm 331, 625, 674.

Zinc phthalocyanine **(1b)**; Yield 280 mg (90%) m.p.> 200 °C. 3440 (NH), 3331 (NH), 3104, 3056, 1598, 1477, 1446, 1444, 1382, 1305, 1096, 1034, 741. ^{1}H-NMR (DMSO-d$_6$) δ, ppm: 7.83-7.81(6H, m, ArCH), 7.709-7.700 (6H, m, ArCH), 7.42-7.40 (6H, m, ArCH) 7.04-7.01 (6H, m, ArCH), 6.85-6.83(6H, m, ArCH), 5.66 (8H, m, NH). Anal. Calcd. For $C_{56}H_{36}N_{12}S_4Zn$: C, 62.82; H, 3.39; N, 15.70 Found: C, 62.69; H, 3.35; N, 15.55. UV/vis (DMSO): λ_{max} /nm 352, 616, 682.

X-Ray diffraction analysis

A suitable crystal of compound **(1)** was selected for data collection which was performed on a Stoe IPDS diffractometer equipped with a graphite-monochromatic Mo-K$_\alpha$ radiation at 296 K. The structure was solved by direct methods using SHELXS-97 [13] and refined by full-matrix least-squares methods on F^2 using SHELXL-97 [13] from within the WINGX [14] suite of software. All non-hydrogen atoms were refined with anisotropic parameters. The H atoms of C atoms were located from different maps and then treated as riding atoms with C-H distances of 0.93-0.97 Å. Molecular diagrams were created using MERCURY [15]. Supramolecular analyses were made and the diagrams were prepared with the aid of PLATON [16]. Details of data collection and crystal structure determinations are given in Table-1.

Table-1: Crystal data and structure refinement parameters for compound **1.**

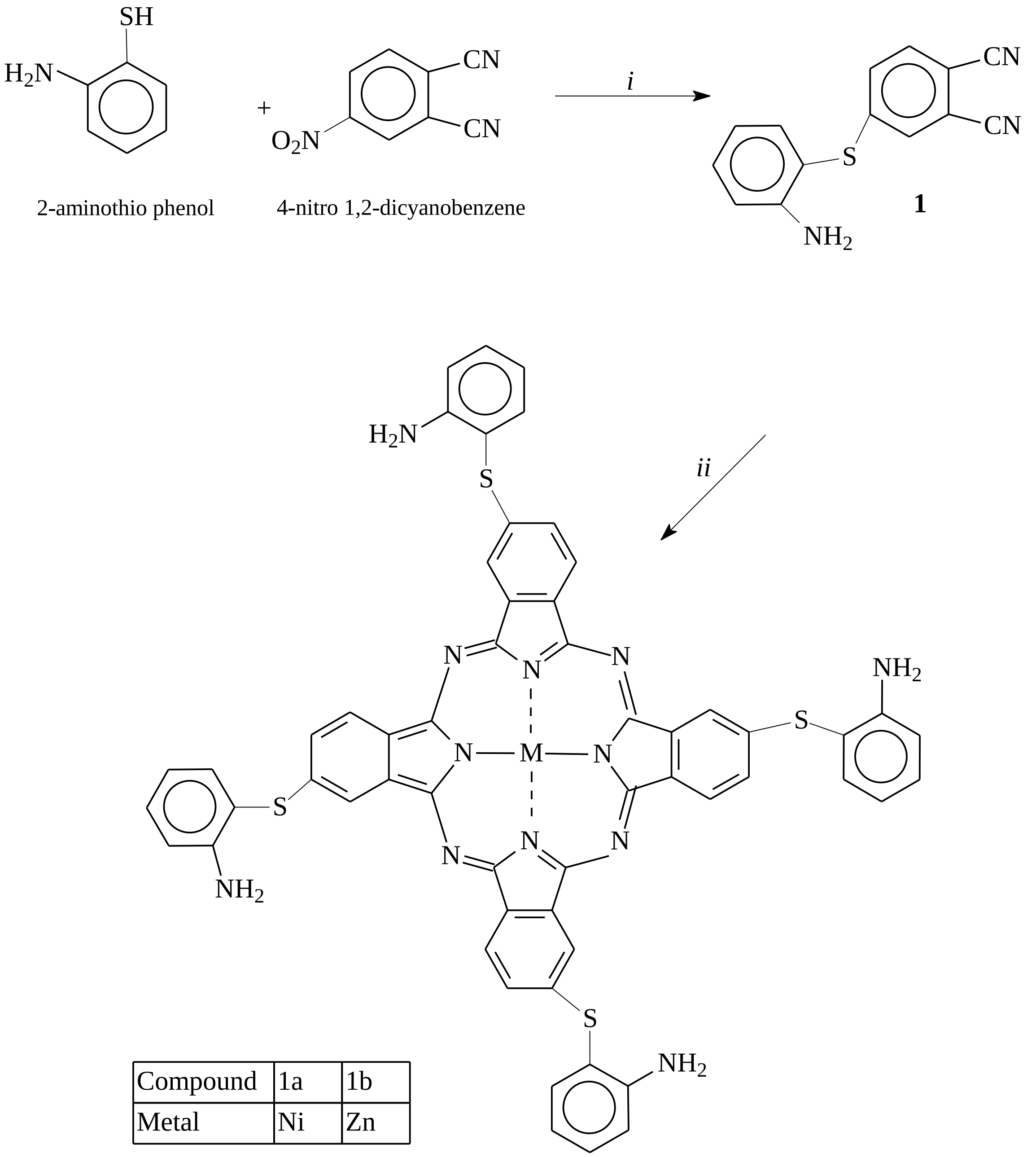
Crystal data	**1**
Empirical formula	$C_{14}H_9N_3S$
Formula weight	**251.30**
Crystal system	**Monoclinic**
Space group	$P2_1/n$
a **(Å)**	**8.7405 (7)**
b **(Å)**	**9.7930 (7)**
c **(Å)**	**14.5275 (12)**
α (°)	**90.00**
β **(°)**	**98.144 (3)**
γ **(°)**	**90.00**
V **(Å^3)**	**1230.95 (17)**
Z	**4**
D_c **(g cm^{-3})**	**1.356**
μ (mm^{-1})	**0.25**
θ range (°)	**3.1-28.2**
Measured refls.	**17054**
Independent refls.	**3051**
R_{int}	**0.037**
S	**1.04**
R1/wR2	**0.053/0.155**
$\Delta\rho_{max}/\Delta\rho_{min}$ **(eÅ^{-3})**	**0.46/-0.41**

Supplementary Material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 1051764 for compound **(1)**. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Results and Discussion

The synthetic path of novel metallophthalocyanines (M: Ni, Zn) can be seen in Scheme-1. 4-Nitro–1,2-dicyanobenzene was prepared according to literature procedure [12]. Phthalonitrile compound **1** was prepared by the treatment of 4-nitro–1,2-dicyanobenzene with 2-aminothiophenol. Then, metallophthalocyanines **1a** and **1b** (M: Ni, Zn) were synthesized using microwave irradiation from the phthalonitrile compound **(1)** and corresponding metal salt in n-hexanol mixture for 20 minutes.



Compound	1a	1b
Metal	Ni	Zn

Scheme-1: Synthesis route of compound **(1)** and metallophthalocyanines **(1a-b)**.

i) K_2CO_3/DMSO, 150 °C, MW, 10 mins. *ii)* Metal salts/Hexanol/DBU, 200 °C, MW, 20 mins.

The characterization of the products involved a combination of methods, including FT-IR, UV/vis, ^{1}H-NMR, ^{13}C-NMR, X-Ray diffraction (just for compound **1**) and elemental analysis.

In the FT-IR spectrum, the formation of compound **1** was clearly indicated by the appearance of NH_2 bands at 3460-3459 and sharp CN band at 2231 cm^{-1}. The formation of compound **1** was signified by the appearance of aromatic peaks at 7.97-6.63 ppm and NH_2 protons at 5.81 ppm as a single, in its ^{1}H-NMR spectrum. The ^{13}C-NMR spectrum of compound **1** showed the presence of nitrile carbon atoms at 116.50 and 116.00 ppm.

FT-IR spectra of the metallophthalocyanines **1a** and **1b** clearly signify the cyclotetramerization of the phthalonitrile derivative **1** with the disappearance of the CN peaks at 2231 cm^{-1}. The ^{1}H-NMR spectra of metallophthalocyanines **1a** and **1b** (M: Ni, Zn) have broader peaks than the starting phthalonitrile compound **1.** Tetra substituted phthalocyanines compounds afford an isomeric mixture contain four possible structural isomers in all cases. The four isomers can be obtained with molecular symmetries D_{2h}:C_{4h}:C_{2v}:C_s in ratio of 1:1:2:4. No attempt has been made to separate the isomers of phthalocyanines.

Elemental analysis results of the starting material **1** and the metallophthalocyanine compounds **1a** and **1b** show good agreement with the calculated values.

The best characteristic for the phthalocyanine compounds is their UV/vis spectra. The electronic spectra of phthalocyanines exhibit two strong absorption regions, one of them is in the UV region, and the other one is in the visible region. Also, the newly synthesized metallophthalocyanines **1a** and **1b** showed typical electronic spectra with two strong absorption regions, one of them in UV region between 331 and 352 nm (B band) and the other in the visible region between 674 and 682 nm (Q band) in DMSO, respectively. The UV/vis spectra of newly synthesized phthalocyanines **1a** and **1b** can be seen in Fig 1. The Q band is attributed to π→π* transitions from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) of the Pc ring. The other bands (B) in the UV region are observed due to the transitions from the deeper π levels to the LUMO [17].

Crystallographic analysis of compound **1**

The molecular structure of compound **1** with the atom labeling is shown in Fig. 2. Both nitriles in the molecule are equivalent and typical of N≡C triple bonds [1.135 (3) Å] (Table-2). The dihedral angles of the phenyl rings is 67.92 (57)°. The molecules of compound **1** are connected by N-H···N hydrogen bonds (Table-3). The intramolecular N1-H1A···S1 hydrogen bond produce S(5) ring. The amino N1 atom acts as hydrogen-bond donor, via atom H1B, to atom N3 in the molecule at (x+1/2, −y+1/2, z−1/2), forming a C(11) chain running which is parallel to the [101] direction (Fig. 3).

Table-2: Selected bond distances and angles for compound 1 (Å, °).

1			
C13-N2	**1.135 (3)**	**C14-N3**	**1.135 (3)**
C6-S1-C7	**104.86 (10)**		

Table-3: Hydrogen bonds parameters for compound 1 (Å, °).

D-H···A	D-H	H···A	D···A	D-H···A
1				
N1-H1A···S1	**0.94 (2)**	**2.49 (4)**	**3.059 (3)**	**119 (4)**
N1-H1B···N3^i	**0.93 (2)**	**2.61 (4)**	**3.439 (4)**	**150 (5)**

Symmetry codes: (i) x+1/2, −y+1/2, z−1/2 for 1

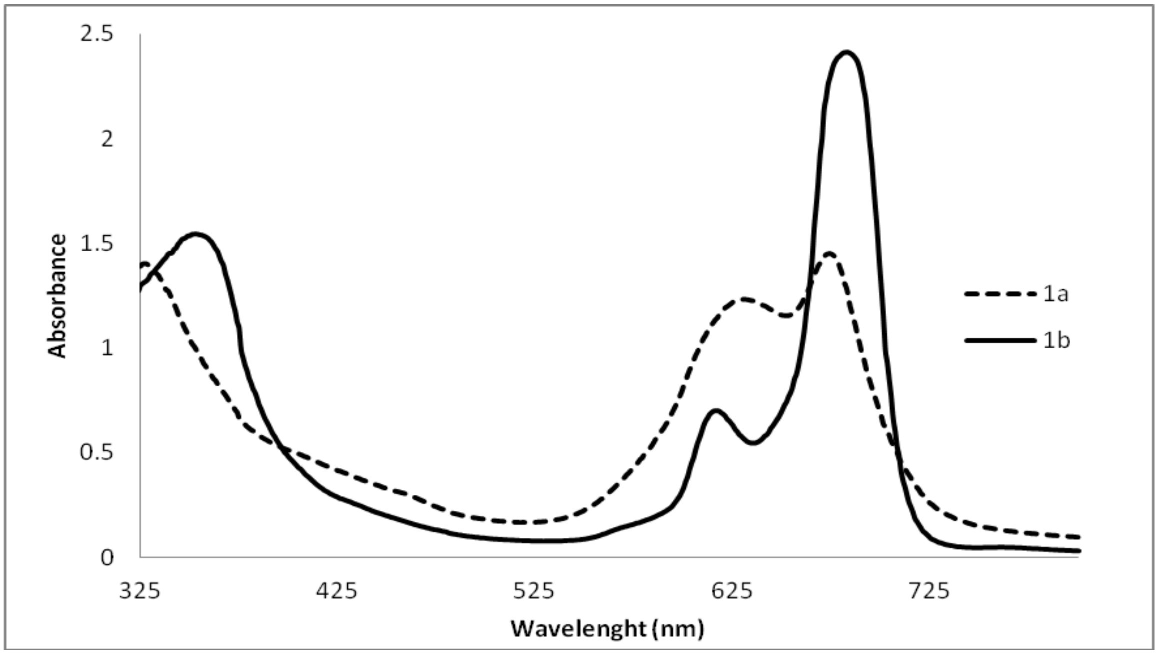


Fig. 1: UV/vis spectra of compounds **1a** and **1b** (in DMSO).

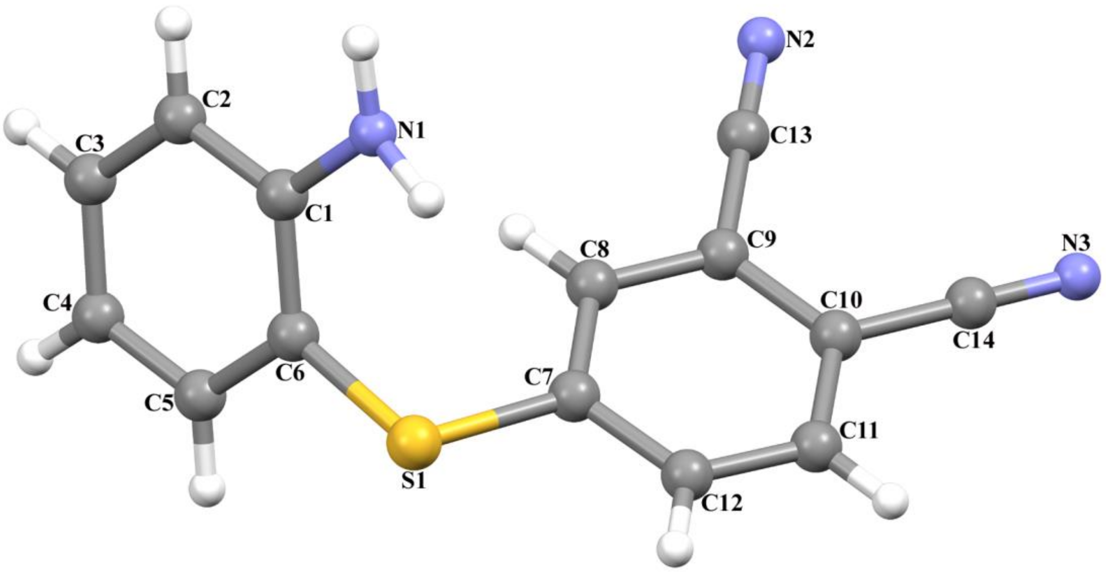


Fig. 2: The molecular structure of compound **1** showing the atom numbering scheme.

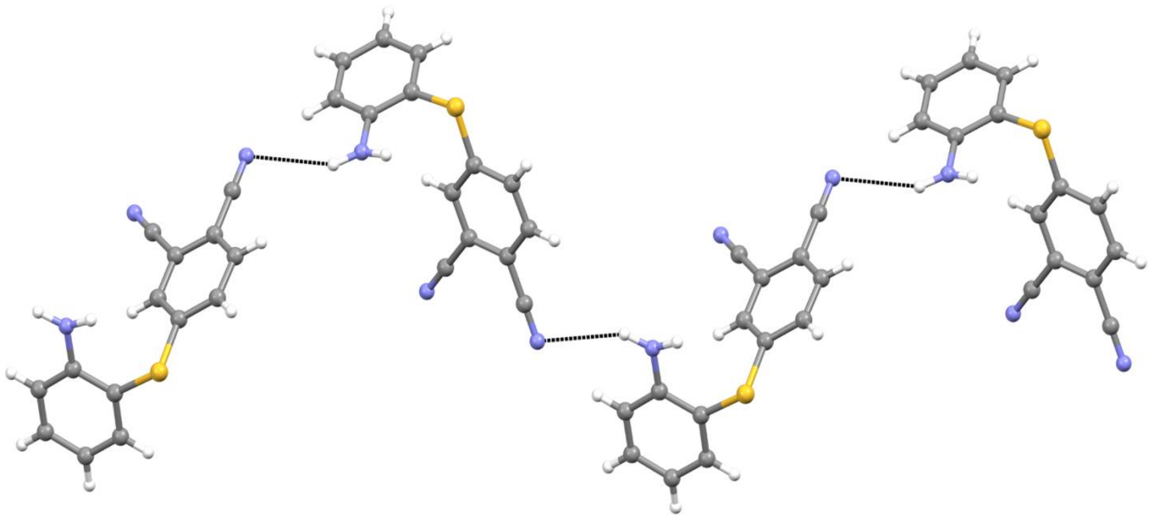


Fig.3: Crystal structure of compound **1**, showing the formation of a chain along [101] generated by N-H···N hydrogen bonds.

Aggregation properties

Aggregation is commonly represented as a coplanar association of rings progressing from monomeric to dimeric and oligomeric complexes. It depends on the concentration, structure of the solvent, orientation of the substituents, complexed metal ions and temperature [18]. Aggregation is an undesirable phenomenon for the PDT applications due to reduce singlet oxygen quantum yield that main therapeutic cytotoxic agent [19, 20]. As seen from Fig 1, the absorption spectra of the examined metallophthalocyanines **1a** and **1b** demonstrated characteristic absorptions in the Q band region at 674 and 682 nm and the B bands at 331 and 352 nm in DMSO, respectively.

The absorption spectra of compounds **1a** and **1b** in DMSO were recorded in the range of 0.25×10^{-4} to 3.25×10^{-6} M, Fig. 4. As the concentration of zinc(II) phthalocyanine **1b** was increased, the intensity of the Q bands increased and any red or blue shift were not observed due to the aggregated species [21]. So, this complex exhibited a monomeric form as deduced from the recorded absorption spectra in different concentrations. The Zinc(II) phthalocyanine **(1b)** did not show high aggregation in DMSO solvent. However, when the concentration of nickel(II)phthalocyanine **1a** was increased, the intensity of the Q bands increased and also intense shoulder peak was observed to shift to red due to the aggregated species (Fig. 4). So, Ni(II)phthalocyanine exhibited an aggregated form as deduced from the recorded absorption spectra in different concentrations. The Ni(II)phthalocyanine **(1b)** shows high aggregation in DMSO. This may be related to be free amino groups at phthalocyanines macrocylic can bind to central Ni(II) atoms by non covalent interactions.

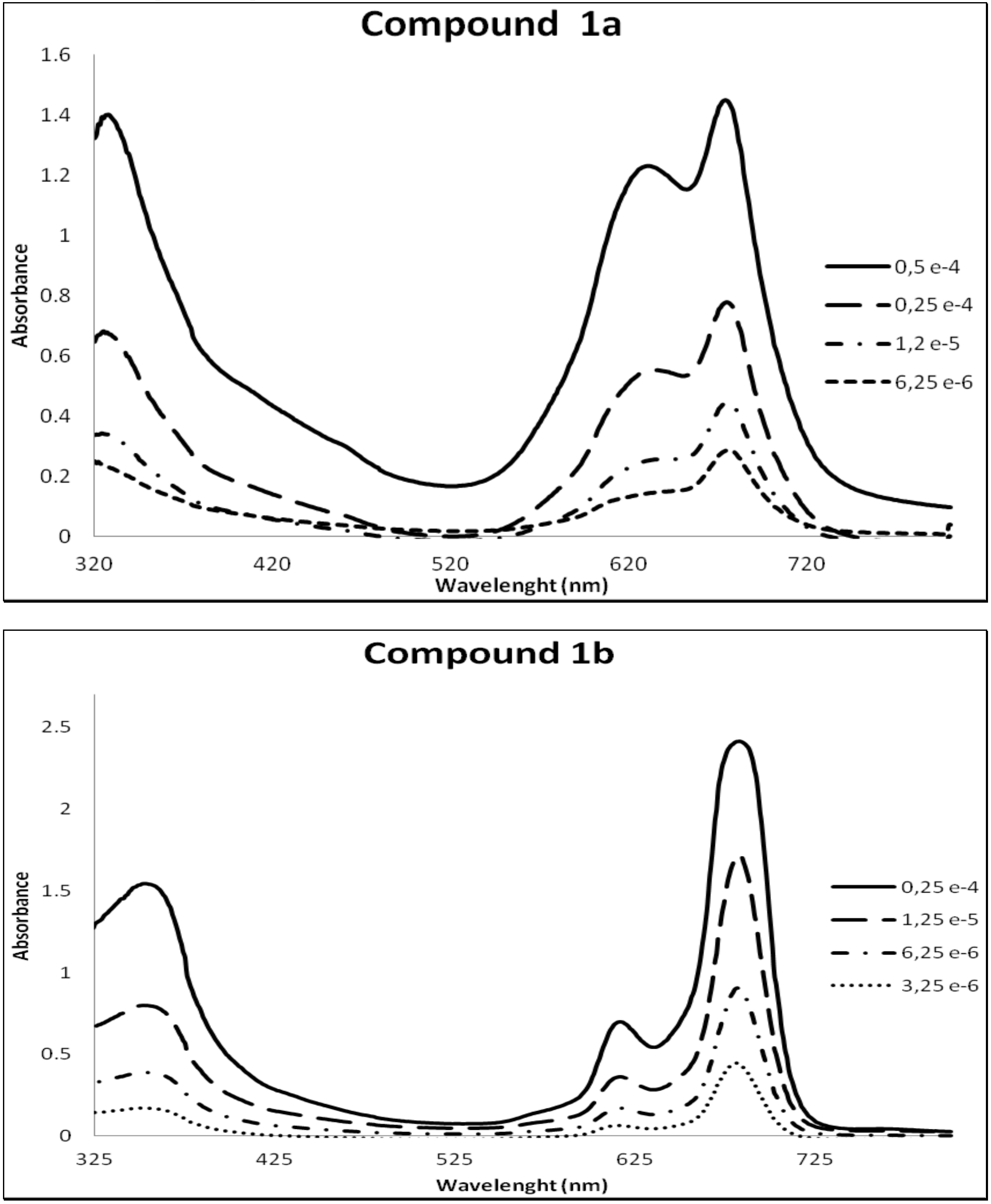


Fig. 4: UV/vis spectra of compounds **1a** and **1b** at different concentrations (in DMSO).

Conclusion

Novel peripherally 2-aminothiophenol substituted metallophthalocyanines were synthesized by a microwave-assisted method. Also, the crystal structure of starting compound **1** was determined. Aggregation behavior of metallophthalocyanines were investigated at different concentration in DMSO and its determined that Ni(II) phthalocyanine showed high aggregation tendency when compared with Zn(II)phthalocyanine. The zinc(II)phthalocyanine compound seems to be suitable for the PDT due to low aggregation tendency and red-shifted Q band absorption. The results of this study provide important information to facilitate the design and synthesis of new thio-substituted phthalocyanine compounds.

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