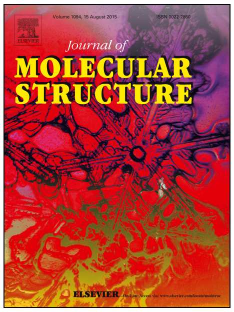

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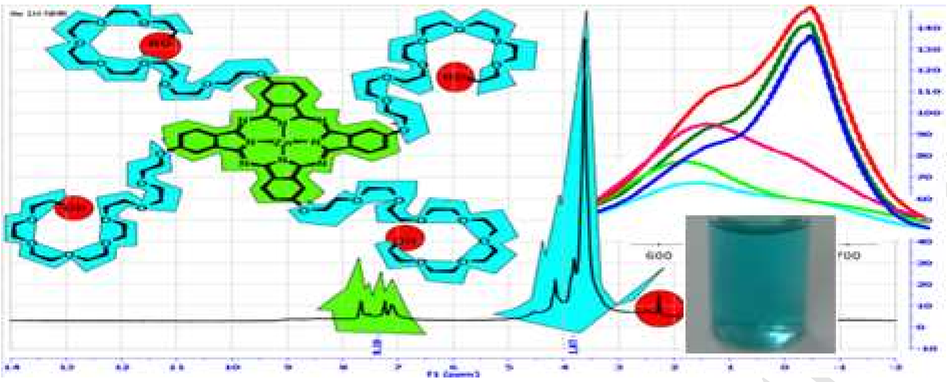
Graphical Abstract (1)



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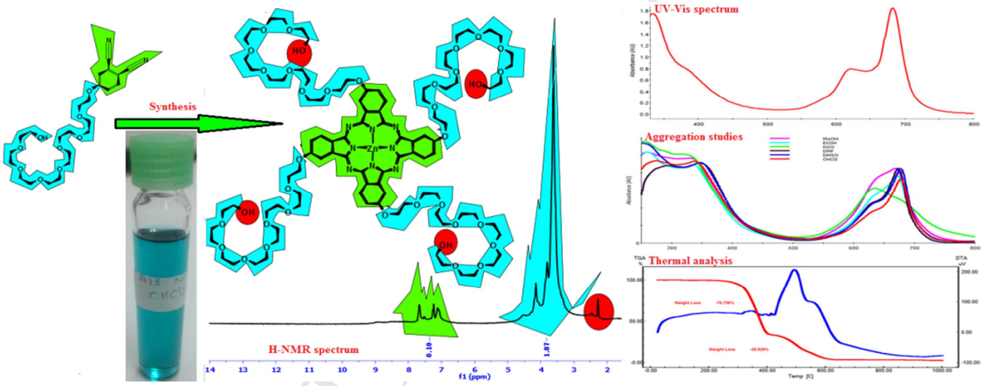
Graphical Abstract (2)



Synthesis, spectroscopic properties, thermal properties and aggregation behaviors of macrogol-substituted phthalocyanines

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Abstract

The synthesis, characterization, spectroscopic data, solubility and aggregation behaviors depend on the solvents of metalled (Co, Cu, Ni, Zn) and metal free pegylated phthalocyanines (Pcs) were reported. Precursor phthalonitrile compound (**4**) for phthalocyanine formation was synthesized by nucleophilic substitution reaction between tetraethylene glycol substituted phthalonitrile (**2**) and tetraethylene glycol monotosylate (**3**). Related phthalocyanines (**4-H**, **4-Co**, **4-Cu**, **4-Ni**, and **4-Zn**) were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, and UV-Vis spectroscopies and elemental analysis. Thermal stabilities of the phthalocyanines were determined in the range between room temperature and 1000 °C. Pegylated phthalocyanines showed high solubility in water and common organic solvents including methanol, ethanol, acetone, pyridine, 1,4-dioxane, dimethylformamide, dimethylsulfoxide, dichloromethane, and chloroform. Aggregation states of all phthalocyanines were investigated in the aforementioned solvents using UV-Vis spectroscopy method. All phthalocyanines were especially found highly aggregated in their aqueous solutions.

Keywords: Phthalocyanine; Macrogol; Phthalocyanine aggregation; Polyethylene glycol; Water solubility; PEGylation

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1. Introduction

Phthalocyanines (Pcs) and their derivatives are one of the most studied subjects in functional material science [1]. Thanks to their constitutional electronic delocalization, they were found useful for many application areas in different fields [2]. Using them as photosensitizer in photodynamic therapy is one of these fields [3] . They are also used in optical data storage, liquid crystals, molecular semiconductors, sensors, photovoltaic devices, electrochromic devices, non-linear optics, fuel cells [4, 5]. However, phthalocyanine compounds have some undesirable properties. First of all they are prone to aggregation [6-8]. Phthalocyanine aggregation is generally defined as coplanar association of the molecules range from monomer to long-range order complexes by means of secondary interactions. In the aggregation state, physical and chemical properties of the molecules change compare to their monomeric state. This aggregation phenomenon is important especially in color, photodynamic activity, catalytic activity and their relevant applications [9]. The aggregation is reducible via different approaches including choosing hydrophilic and amphiphilic groups such as carboxylates, sulfonates, phosphonates, PEGs, and bulky axial substituents at phthalocyanine macrocyclic [10]. Another problem related to phthalocyanines is solubility [7, 11]. The solubility can be increased with bonding to phthalocyanine of carboxylates, sulfonates, quaternized amino and pyridine groups[12-14]; hydroxyl group, peptides, oligonucleotides and polyethylene glycol (PEG) groups [13, 14].

Polyethylene glycol, PEG, is a synthetic polymer composed of ethylene oxide monomers. PEG is nontoxic, nonimmunogenic, nonantigenic, amphiphilic and FDA approved in different pharmaceutical applications [15]. Pegylation is defined in different ways by different groups [15-19]. Most comprehensive definition of pegylation is bound of polyethylene glycols to molecules that changing from drugs to macromolecules via covalent or non-covalent interactions [20]. Pegylated molecules have many advantages compare to non-pegylated counterparts: increased half-life in body and thus, enhanced bioavailability [15, 17, 21-23], solubility in aqueous medium [21, 23], decreased immunogenicity [15, 17, 21, 23], protection against enzymatic degredation and reticuloendothelial cells [15, 19, 21, 22], improved tumour targeting [17, 21], decreased aggregation and increased thermal stability [18].

Directly or indirectly pegylated phthalocyanines have been synthesized by different groups [12-14, 24-30]. Our aim in this study is to synthesize of pegylated phthalocyanines with PEG

400 (belong to family of macrogol or polyethylene glycol), to investigate their aggregation behaviors in different solvents and to determine their thermal stabilities.

2. Experimental

2.1. Materials

Tetraethylene glycol (TEG), absolute methanol and ethanol, chloroform, dichloromethane, hexane, diethyl ether, ethyl acetate, tetrahydrofuran, dimethylformamide, dimethylsolfoxide, all metal salts ($Zn(CH_3COO)_2$, $NiCl_2$, $CuCl_2$, $CoCl_2$), anhydrous sodium sulfate, anhydrous magnesium sulfate, phthalimide and ammonia solution (25%) were purchased from Sigma-Aldrich. HCl solution (37-38%) was supplied from J.T. Baker. 1-Pentanol was supplied from Honeywell Riedel de Haën. Sodium hydride (60% dispersion in mineral oil) was purchased from ACROS Organics. TLC Plates (Silica Gel 60 F 254) were purchased from Merck. Flash column chromatography was performed on silica gel (200–400 mesh particle size, from Sigma Aldrich). Compounds 1 [31], 2 [27] and 3 [32] were synthesized according to the given articles.

2.2. Equipment

Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR) were recorded on Agilent Technologies 400/54/ASP Magnet spectrometer. Elemental analysis results were obtained from Thermo Scientific Flash 2000 instrument. FTIR spectra were recorded on Perkin-Elmer spectrum version 10.03.06. TGA measurements were performed by Shimadzu DTG 60/60H TG/DTA simultaneous measuring instrument. Melting points were measured by using Stuart SMP 30 instrument. UV-Vis spectra were recorded on Thermo Scientific evolution array UV-Vis spectrophotometer. TLC plates were visualized by CAMAG UV Cabinet 4. All samples were weighed by the electronic single pan balance, Precisa XB 220A. Elektro-Mag M 6040 P Sterilizer was used for drying procedures. A Heidolph MR Hei-Standard hot plate was used to control the temperatures.

2.3. Synthesis

2.3.1. 4-(23-hydroxy-3,6,9,12,15,18,21-heptaoxatricosyloxy)phthalonitrile (**4**)

A solution of NaH (60% dispersion in mineral oil) (0.48 g, 11 mmol) in THF (30 mL) was cooled down to 0 °C. A solution of compound **2** (3.5 g, 11 mmol), 4-(2-(2-(2-(2-

hydroxyethoxy)ethoxy)ethoxy)ethoxy)phthalonitrile, in THF (30 mL) was added drop by drop to NaH solution and the mixture was stirred for two hours at the same temperature. A solution of compound **3** (3.83 g, 11 mmol), 2-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethyl 4-methyl benzenesulfonate, in THF (10 mL) was added drop by drop to the solution and the mixture was stirred for ten hours. At the end of time, the mixture was warmed to room temperature. The reaction mixture was filtered and all volatile compounds were removed by rotary evaporation. The recovered product was solved in toluene and the organic layer was extracted with distilled water (3x10 mL). The aqueous layer was extracted with chloroform (3x10 mL). The remaining organic layer was dried with $MgSO_4$. The solvent was removed by rotary evaporation. The product was obtained as a yellow and oily compound.

Yield: 39% (2.1 g), R_f: 0.75 (dichloromethane/methanol, 1:1, v/v), FTIR (ATR), ν/cm^{-1}: 3500-3200 (OH), 3097 (Ar. C-H), 2975, 2870 (Al. C-H), 2226 (CN), 1590, 1560, 1490, 1450 (C=C), 1245, 1178, 1100 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$) (δ: ppm): 7.64 (dd, 1H, Ar-H), 7.17 (d, 1H, Ar-H), 7.05 (d, 1H, Ar-H), 4.24-3.00 (m, 32H, O-CH_2CH_2-O), 2.32(s, b, 1H,-OH). ^{13}C NMR (101 MHz, $CDCl_3$) (δ: ppm): 61.14, 68.38, 69.41-72.88, 106.9, 115.4, 115.8, 116.8, 119.87, 119.6, 135.0, 161.9.

2.3.2. Synthesis procedure of metalled and metal-free phthalocyanines

Pegylated phthalonitrile (**4**), (0.3 g, 0.6 mmol) was stirred in pentanol at 60 °C under nitrogen atmosphere for 30 minutes and later on, metal salt, except metal-free phthalocyanine, [$CoCl_2$ (0.039 g, 0.3 mmol), $CuCl_2$ (0.04 g, 0.3 mmol), $NiCl_2$ (0.039 g, 0.3 mmol), $Zn(OAc)_2$ (0.055 g, 0.3 mmol)] and DBU(0.23 mL, 1.5 mmol) were added. The final mixture was heated to reflux temperature and stirred under nitrogen atmosphere for 48 h. Pentanol was removed under reduced pressure. The recovered product was dissolved in chloroform (10 mL) and extracted with distilled water (3x10 mL). The organic layer was dried with sodium sulfate overnight. The solvent was removed by rotary evaporation. Bluish green compound was washed with ether and ethyl acetate. The colored compound was purified by flash column chromatography on silica gel with dichloromethane, dichloromethane/methanol (92:8, v/v) as eluent, respectively. All volatile organic compounds were removed in vacuum. The bluish green solid was dried at 120 °C.

Pegylated metal free phthalocyanine (**4-H**): Yield: 12.4% (0.037 g), FTIR (ATR), ν/cm^{-1}: 3385, 3211 (-OH); 3075 (Ar. CH), 2921, 2871 (Al. CH), 1660, 1606, 1523, 1451 (C=C, C=N), 1239 (Ar-O-C), 1094, 1066 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$) (δ: ppm): 2.28 (s, b, 4H,-OH); 3.25-4.80 (m, 128H, OCH_2CH_2O); 6.82-7.87 (m, 12H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) (δ: ppm): 61.63, 69.35, 70.26-70.76, 72.49, 125.87, 128.78, 130.89. Elemental analysis: Anal. Calcd for $C_{96}H_{146}N_8O_{36}$ (%): C 57.99, H 7.40, N 5.64. Found: C 57.84, H 7.43, N 5.66. UV-Vis ($CHCl_3$), λ_{max} nm (logε): 699 (5.00), 675 (5.10), 642 (4.82), 614 (4.72), 374 (5.03).

Pegylated cobalt phthalocyanine (**4-Co**): Yield: 9% (0.027 g), FTIR (ATR), ν/cm^{-1}: 3391(-OH); 2921, 2872 (Al. CH), 1662, 1609, 1455 (C=C, C=N), 1241 (Ar-O-C), 1095, 1067 (C-O-C). Elemental analysis: Anal. Calcd for $C_{96}H_{144}N_8O_{36}Co$ (%): C 56.38, H 7.10, N 5.48. Found: C 56.33, H 7.11, N 5.50. UV-Vis ($CHCl_3$), λ_{max} nm (logε): 674 (3.99), 614 (3.55), 309 (4.29).

Pegylated copper phthalocyanine (**4-Cu**): Yield: 27% (0.07 g), FTIR (ATR), ν/cm^{-1}: 3391, 3195 (-OH); 3053(Ar. CH), 2921 (Al. CH), 1651, 1610, 1438 (C=C, C=N), 1244 (Ar-O-C), 1097, 1063 (C-O-C). Elemental analysis: Anal. Calcd for $C_{96}H_{144}N_8O_{36}Cu$ (%): C 56.25, H 7.08, N 5.47. Found: C 56.22, H 7.10, N 5.49. UV-Vis ($CHCl_3$), λ_{max} nm (logε): 682 (4.56), 621 (4.20), 380 (4.21), 334 (4.54).

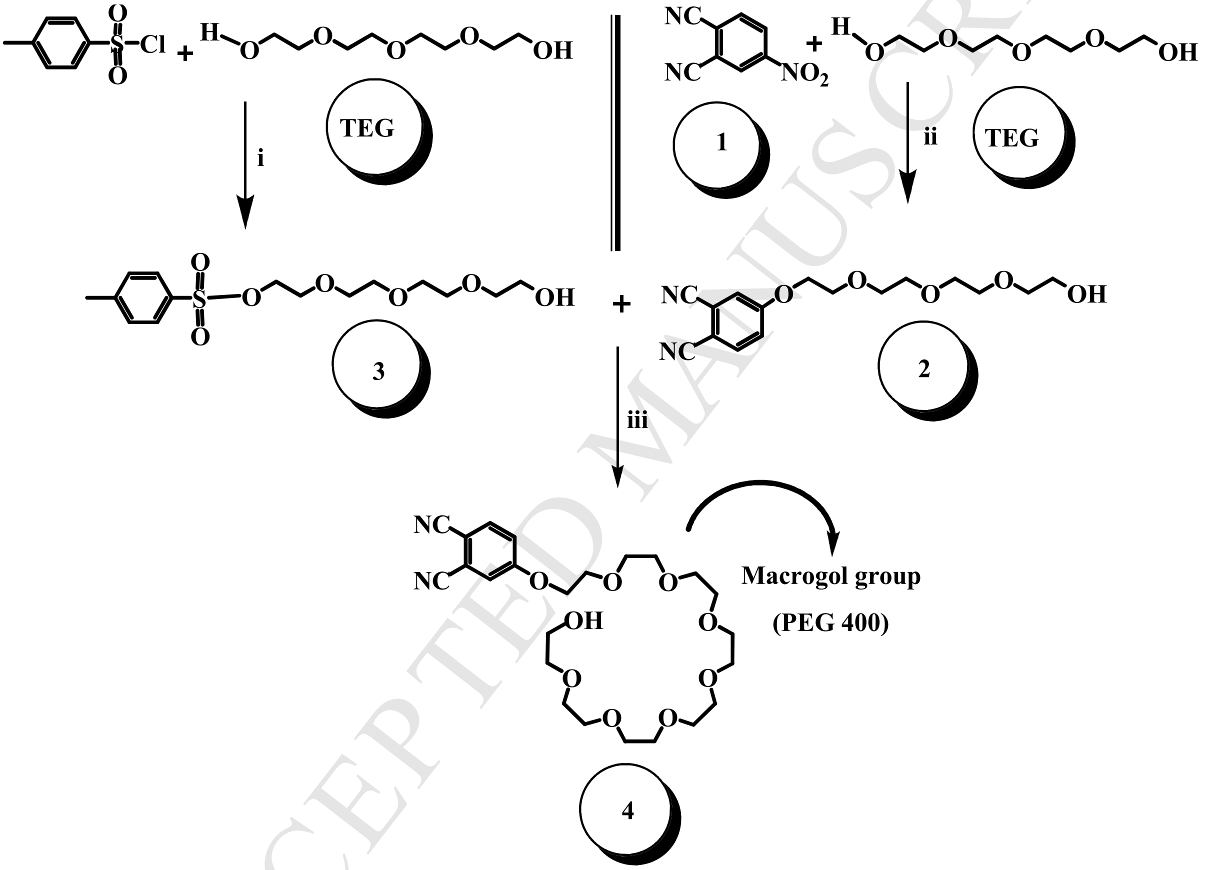
Pegylated nickel phthalocyanine (**4-Ni**): Yield: 20% (0.06 g), FTIR (ATR), ν/cm^{-1}: 3373, 3205 (-OH); 2923, 2870 (Al. CH), 1660, 1609, 1453 (C=C, C=N), 1242 (Ar-O-C), 1094, 1066 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$) (δ: ppm): 1.67 (s, b, 4H,-OH); 2.84-4.51(m, 128H, OCH_2CH_2O); 7.02-8.00 (m, 12H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) (δ: ppm): 61.50, 68.28, 69.34, 69.69-70.99, 72.77. Elemental analysis: Anal. Calcd for $C_{96}H_{144}N_8O_{36}Ni$ (%): C 56.39, H 7.10, N 5.48. Found: C 56.37, H 7.11, N 5.50. UV-Vis ($CHCl_3$), λ_{max}, nm (logε): 674 (4.35), 621 (4.02), 372 (3.62).

Pegylated zinc phthalocyanine (**4-Zn**): Yield: 14% (0.042g), FTIR (ATR), ν/cm^{-1}: 3391, 3212 (-OH); 3071 (Ar. CH), 2917, 2872 (Al. CH), 1664, 1607, 1487, 1450 (C=C, C=N), 1232(Ar-O-C), 1092, 1059 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$) (δ: ppm): 2.27 (s, b, 4H,-OH); 3.20-4.74 (m, 128H, OCH_2CH_2O); 6.88-7.80 (m, 12H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) (δ: ppm): 61.50, 68.21, 69.27, 70.19-70.77, 72.42, 108.54, 109.99, 120.66, 124.61, 125.12, 125.93, 128.55, 128.78, 130.90, 135.09, 139.54, 163.90, 167.90, 167.96. Elemental analysis: Anal. Calcd for $C_{96}H_{144}N_8O_{36}Zn$ (%): C 56.20, H 7.07, N 5.46. Found: C 56.18, H 7.08, N 5.48. UV-Vis ($CHCl_3$), λ_{max} nm (logε): 683 (3.70), 617 (3.08), 337 (3.71).

3. Results and discussion

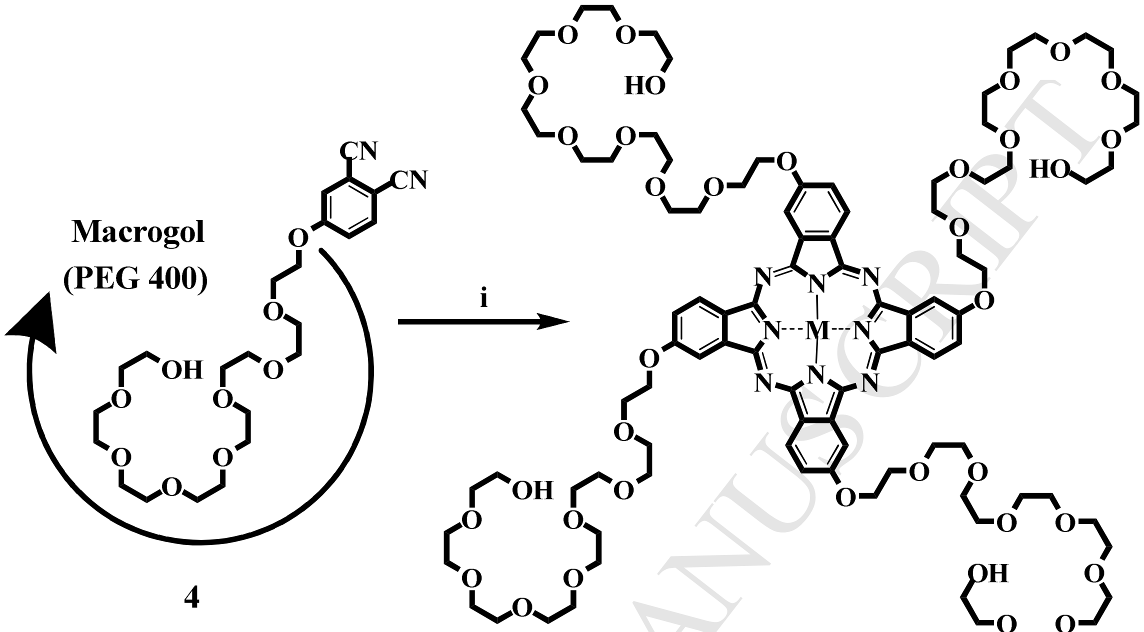
3.1. Synthesis and characterization

Pegylated phthalonitrile derivative (**4**) was synthesized via nucleophilic substitution reaction between 4-(2-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethoxy)phthalonitrile (**2**) and 2-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethyl 4-methyl benzenesulfonate (**3**) in 39% yield. Precursor molecules **1**, **2** and **3** for this reaction were synthesized as given in [27], [31] and [32], respectively. The synthesis routes of these compounds were given in scheme 1.



Scheme 1. Synthesis routes to 2, 3, and 4 numbered compounds. (i) NaOH, THF, 2h and 0 °C. (ii) K_2CO_3, DMF, N_2, 15h and 105 °C. (iii) NaH, THF, 9h and 0 °C.

Five phthalocyanine compounds including metal free, cobalt, copper, nickel, and zinc phthalocyanines were synthesized by cyclotetramerization reaction of pegylated phthalonitrile (**4**) in the presence of n-pentanol as the solvent, DBU as the catalyzer and corresponding anhydrous metal salt under the nitrogen atmosphere. The synthesis routes of these compounds were given in scheme 2. The compounds were obtained as bluish green solids, 12.3%, 9%, 27%, 20%, 14% in yields for **4-H**, **4-Co**, **4-Cu**, **4-Ni**, **4-Zn**, respectively. All compounds were characterized by suitable characterization techniques including FTIR, UV-Vis, ^{1}H NMR, ^{13}C NMR, elemental analysis. Main findings were found suitable for proposed compounds.



M: 2H (4-H), Co (4-Co), Cu (4-Cu), Ni (4-Ni), Zn (4-Zn)

Scheme 2. Synthesis route to the pegylated metal free and metalled phthalocyanines. (i) n-pentanol, DBU, N_2, 48 h, reflux (common for **4-H, 4-Co, 4-Cu, 4-Ni, 4-Zn**) and $CoCl_2$ (for **4-Co**), $CuCl_2$ (for **4-Cu**), $NiCl_2$ (for **4-Ni**), $Zn(OAc)_2$ (for **4-Zn**).

In the FTIR spectrum of the pegylated phthalonitrile (**4**), the broad peak between 3500 and 3200 cm^{-1} points at the presence of OH, the peak at 3097 cm^{-1} points at the presence of aromatic protons, the peaks at 1590, 1560, 1490, 1450 cm^{-1} points at the presence of aromatic C=C bonds, the peaks at 2975, 2870 cm^{-1} and at 1245, 1175, 1108 cm^{-1} points at the presence of aliphatic proton and different C-O-C bonds in the pegylated molecule. Additionally, very sharp peak at 2226 cm^{-1} indicates the presence of CN bonded to the aromatic ring. In the ^{1}H-NMR spectrum of the phthalonitrile derivative, the aromatic protons were observed at 7.64 (dd), 7.17 (d), 7.05 (d) ppm for three different aromatic protons in the aromatic ring. Methylene protons of PEG chain in the molecule were observed from 3.00 ppm to 4.24 ppm as a sharp multiplet peak because of its asymmetric bonding to phthalonitrile. Hydroxyl peak of the molecule was observed broad shaped at 2.32 ppm. In the ^{13}C NMR spectrum of the same compound, the peaks at 115.4 and 115.8 ppm belong to carbon atoms of CN groups. It confirms clearly the presence of the CN groups in the related molecule. The peak groups between 72.88 - 61.4 ppm belong to oxyethylene carbons in the pegylated molecule. The peaks at 161.9, 135.0, 119.6, 119.87, 116.8 and 106.9 ppm belong to six different aromatic carbons in the molecule.

FTIR spectrum of **4-H** (metal free phthalocyanine) showed all functional group peaks in the molecule. Aromatic carbon peaks couldn’t be clearly observed there. The peak at 3385 cm^{-1} together with the shoulder at 3211 cm^{-1} is the signal of OH. The peak at 3075 cm^{-1} is the signal of Ar-H. The peaks at 2921 and 2871 cm^{-1} are signals of aliphatic protons. The peaks at 1660, 1606, 1523 and 1451 are signals of C=C and C=N double bond and finally, the peaks at 1239, 1094, 1066 are signal of different C-O vibrations in the molecule. Additionally, the disappearance of CN peak in the FTIR spectrum of **4-H** is related to the formation of phthalocyanine macrocycle and it confirms that phthalocyanine synthesis was successful. ^{1}H NMR spectrum of this compound shows three different peak groups concerning to aromatic protons, aliphatic protons, and hydroxyl proton at 7.87-6.82, 4.80-3.25 and 2.28 ppm, respectively. ^{13}C NMR spectrum of this compound shows oxyethylene carbon peaks range from 61.63 ppm to 72.49 ppm and some aromatic carbon peaks at 125.87, 128.78, and 130.89 ppm as minor peaks. In the ^{13}C NMR of **4-H**, differentiation of carbon peaks in comparison to compound 4 is also an evidence of phthalocyanine formation. Phthalocyanines are well known their characteristic absorption bands in UV-Vis spectrum. These bonds are known as Q and B bands. The Q bands are seen in the red side of the visible region and relevant to n-π^* electronic transitions; the B bands are seen in the near UV and relevant to π- π^* electronic transitions [33]. Metal free phthalocyanines due to their symmetry (D_{2h}) give two bands known as Q_x and Q_y in the Q band region [34]. In the UV-Vis spectrum of **4-H**, these bands are seen at 699 and 675 nm in response to the Q_x and Q_y, respectively and at 374 nm in response to the B band. UV-Vis spectrum of **4-H** has been obtained in chloroform at $1x10^{-5}$ M as given in Fig. 1. This electronic data are a sign to the presence of NH protons in phthalocyanine center and the formation of the related phthalocyanine.

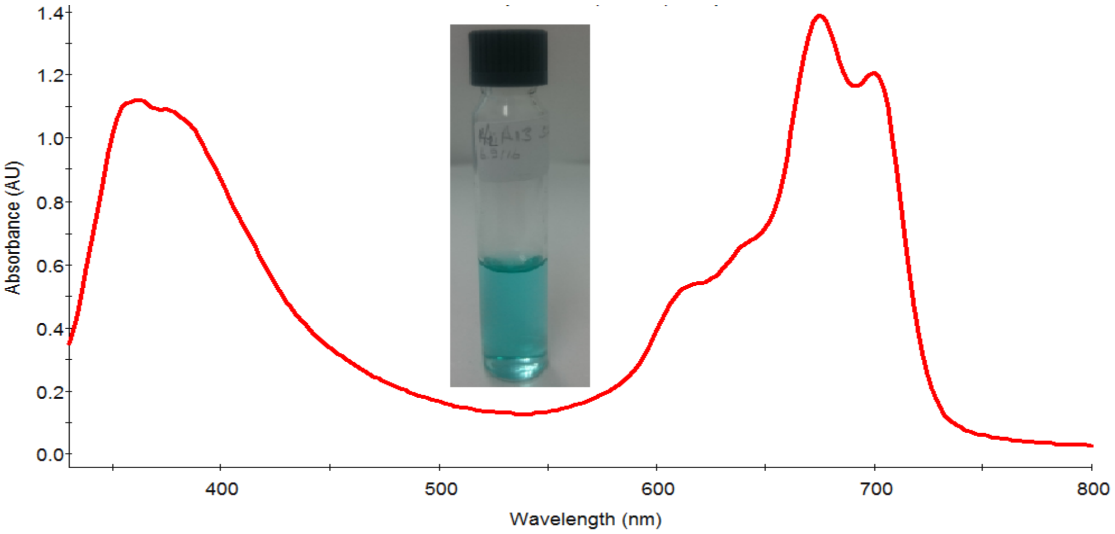


Fig. 1. UV-Vis spectrum of **4-H** in chloroform at 1x10^{-5} M.

In the FTIR spectrum of **4-Co** (pegylated cobalt phthalocyanine), the peak at 3391 cm^{-1} belongs to OH, the peaks at 2921 and 2822 cm^{-1} belong to Al-H, the peaks at 1662, 1609, 1455 cm^{-1} belong to C=N and C=C, the peaks at 1241, 1095 and 1067 cm^{-1} belong to C-O-C (Related spectrum was given in Fig.3 as an example to the synthesized phthalocyanines). Characteristic bands for UV-Vis spectrum of the metalled phthalocyanine were seen at 674 with the shoulder at 614 nm in response to the Q band and at 309 nm in response to the B band. UV-Vis spectrum of **4-Co** has been obtained in chloroform at 5x10^{-5} M as given in Fig. 2.

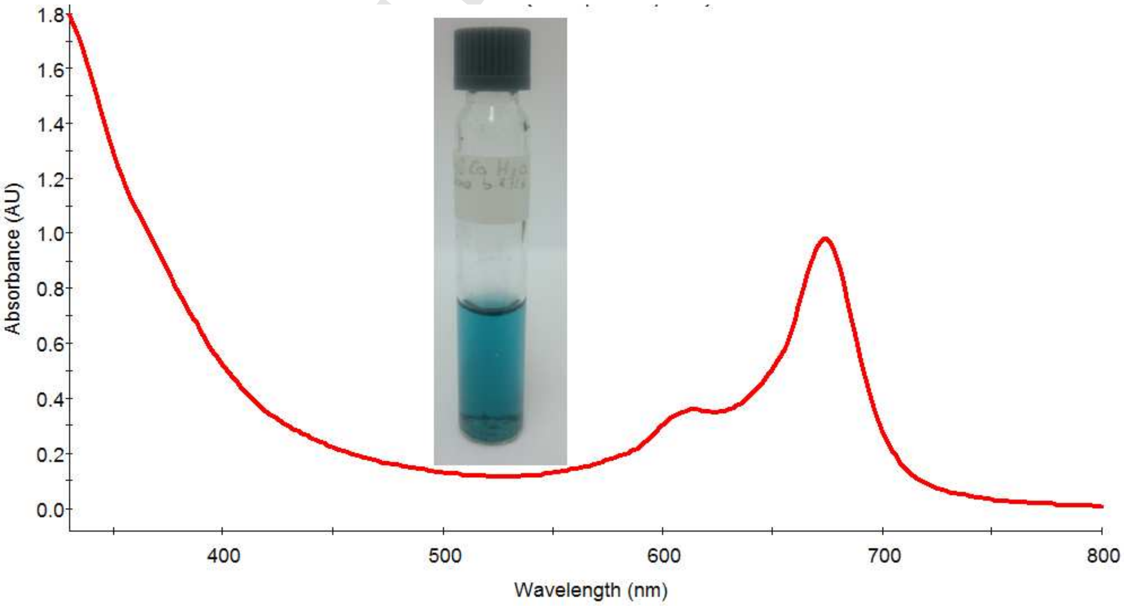


Fig. 2. UV-Vis spectrum of **4-Co** in chloroform at 5x10^{-5} M.

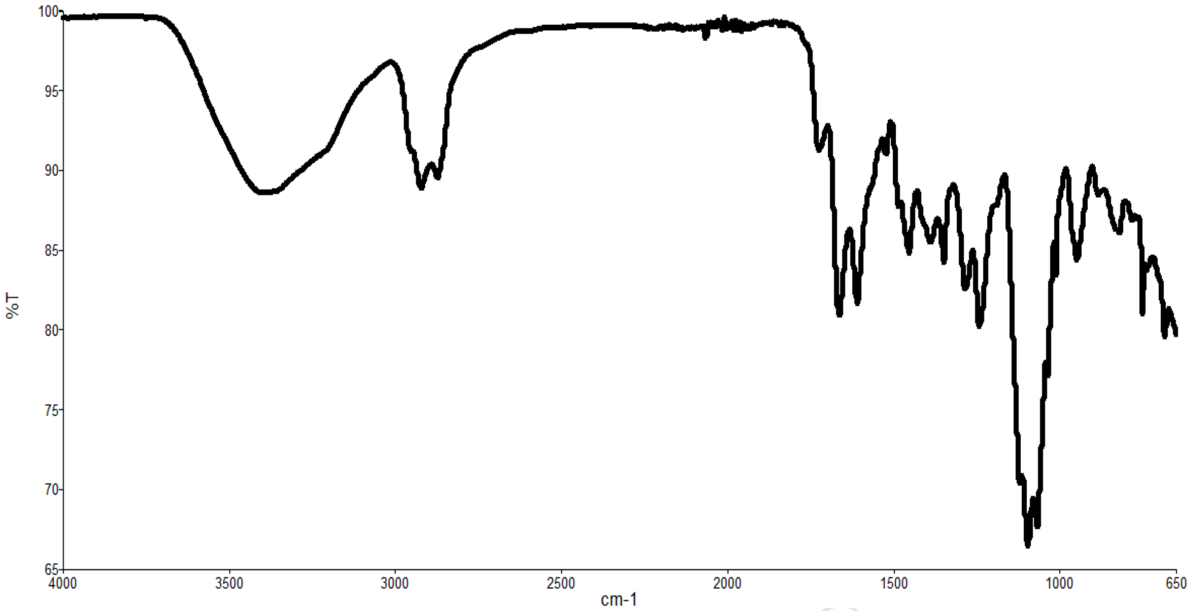


Fig. 3. FTIR spectrum of **4-Co**

In the FTIR spectrum of **4-Cu** (pegylated copper phthalocyanine), the peaks at 3391 and 3195 cm^{-1} belong to OH, the peak at 3053 cm^{-1} belongs to Ar-H, the peak at 2921 cm^{-1} belongs to Al-H, the peaks at 1651, 1610, 1438 cm^{-1} belong to C=N and C=C, the peaks at 1244, 1097 and 1063 cm^{-1} belong to C-O-C. Characteristic bands for UV-Vis spectrum of the metalled phthalocyanine were seen at 682 and 621 nm in response to the Q band and at 380 and 334 nm in response to the B band. UV-Vis spectrum of **4-Cu** has been obtained in chloroform at 5x10^{-5} M as given in Fig. 4.

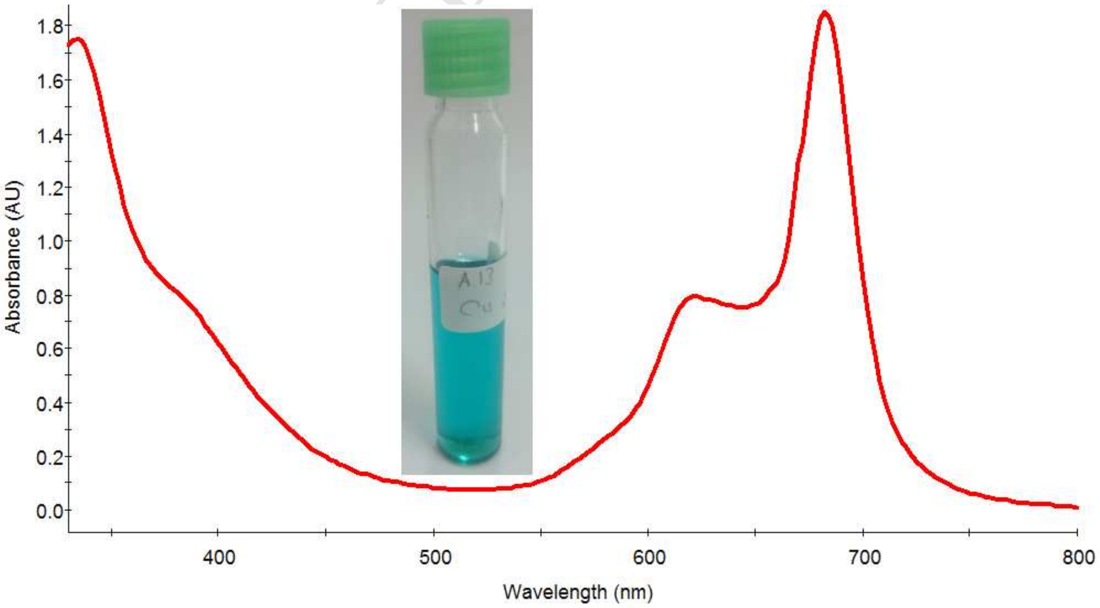


Fig. 4. UV-Vis spectrum of **4-Cu** in chloroform at 5x 10^{-5} M.

FTIR spectrum of **4-Ni** (pegylated nickel phthalocyanine) showed all functional group peaks in the molecule. The peak at 3373 cm^{-1} with the shoulder at 3205 cm^{-1} is signal of OH. The peaks at 2923 and 2870 cm^{-1} are signal of aliphatic protons. The peaks at 1660, 1609, 1453 are signal of C=C and C=N double bond and finally, the peaks at 1242, 1094, 1066 are signal of different C-O vibrations in the molecule. ^{1}H NMR spectrum of this compound shows three different peak groups concerning with aromatic protons, aliphatic protons, and hydroxyl proton at 8.00-7.02, 4.51-2.84 and 1.67 ppm, respectively. ^{13}C NMR spectrum of this compound shows oxyethylene carbon peaks range from 61.50 ppm to 72.77 ppm. Aromatic carbon peaks were not observed due to paramagnetic contrubition of nuclear relaxation. In the UV-Vis spectrum of **4-Ni**, the Q band is seen at 674 with the shoulder at 621 nm and the B band is seen at 372 nm. UV-Vis spectrum of **4-Ni** has been obtained in chloroform at 5x10^{-5} M as given in Fig. 5.

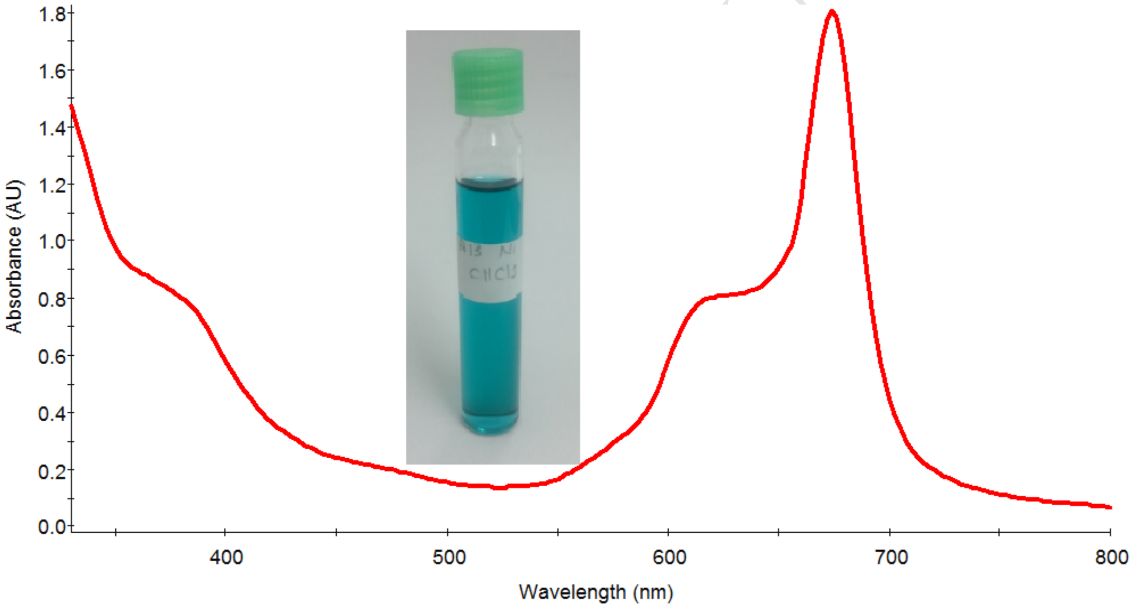


Fig. 5. UV-Vis spectrum of **4-Ni** in chloroform at 5x 10^{-5} M.

FTIR spectrum of **4-Zn** (pegylated zinc phthalocyanine) showed all functional group peaks in the molecule. The peak at 3391 cm^{-1} with the shoulder at 3212 cm^{-1} is signal of OH. The peak at 3071 is signal of aromatic protons. The peaks at 2917 and 2872 cm^{-1} are signal of aliphatic protons. The peaks at 1664, 1607, 1487, 1450 are signal of C=C and C=N double bond and finally, the peaks at 1232, 1092, 1059 are signal of different C-O vibrations in the molecule. ^{1}H NMR spectrum of this compound shows three different peak groups concerning with aromatic protons, aliphatic protons and hydroxyl proton at 7.80-6.88, 4.74-3.20 and 2.27 ppm, respectively. Related spectrum was given in Fig.7 as a sample spectrum for the pegylated phthalocyanines. ^{13}C NMR spectrum of this compound shows oxyethylene carbon peaks range from 61.50 ppm to 72.42 ppm and aromatic carbon peaks range from 108.54 ppm to 167.96 ppm. In the UV-Vis spectrum of **4-Zn**, the Q band is seen at 683 with the shoulder at 617 nm and the B band is seen at 337 nm. UV-Vis spectrum of **4-Zn** has been obtained in chloroform at $1x10^{-4}$ M as given in Fig. 6.

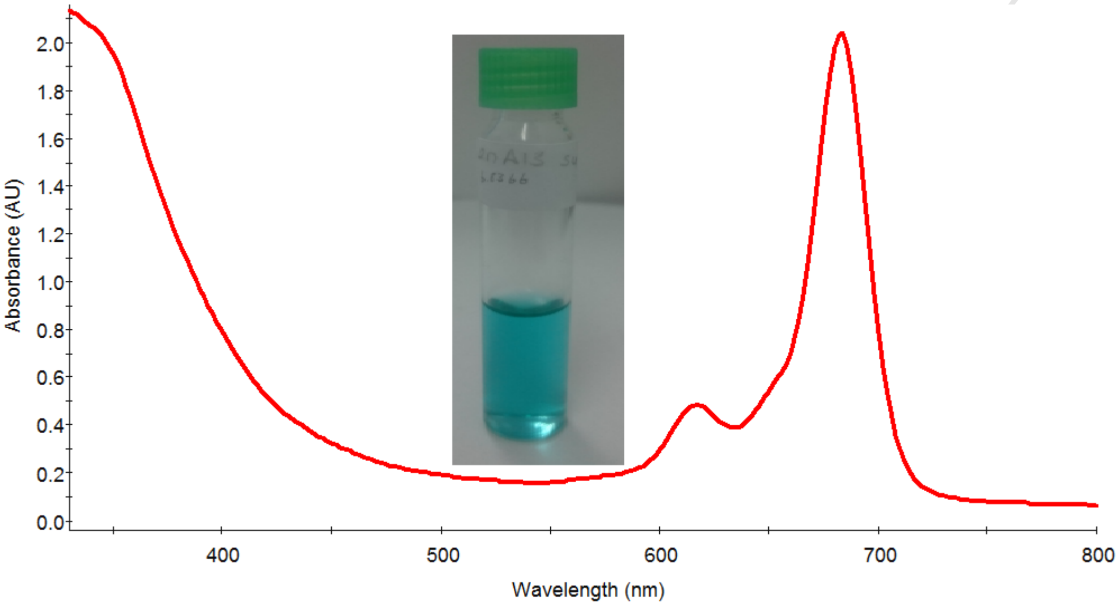


Fig. 6. UV-Vis spectrum of **4-Zn** in chloroform at $1x10^{-4}$ M.

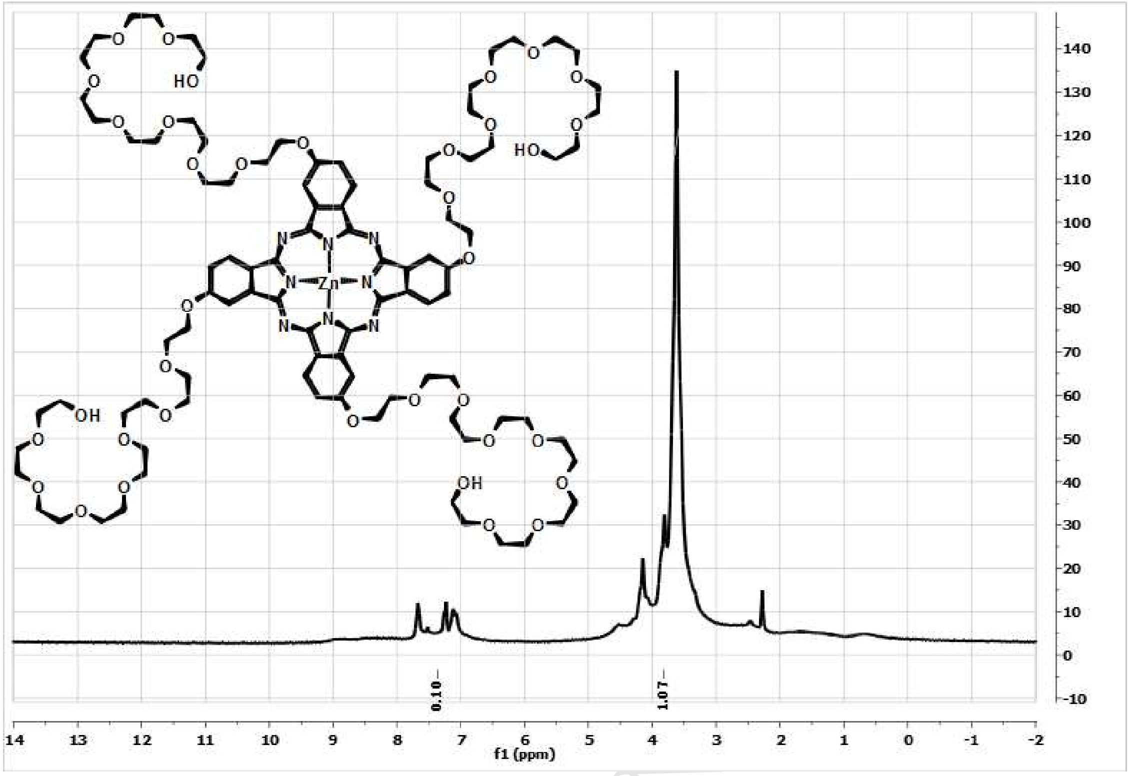


Fig. 7. ^{1}H NMR spectrum of **4-Zn** in $CDCl_3$

3.2. Aggregation Studies

Aggregation is an important phenomenon in phthalocyanine chemistry. Phthalocyanines in the aggregated state have different properties from nonaggregated phthalocyanines [9, 35, 36]. Aggregation behaviors of phthalocyanines as a photosensitizer are a particularly important problem in photodynamic therapy studies. Aggregation decreases their photochemical and photophysical properties [37-39]. Aggregation behaviors of the synthesized compounds were determined by using electronic spectroscopy and investigated depending on solvents in different solvents including chloroform, dimethylformamide, dimethylsulfoxide, ethanol, methanol, and water. The related results were given in Fig. 8 for **4-H**, 9 for **4-Co**, 10 for **4-Cu**, 11 for **4-Ni**, 12 for **4-Zn**. Also, the aggregation behaviors based on concentration for **4-Cu** and **4-Ni** were investigated in foregoing solvents. The results of the latter study were given in Fig. 13 for **4-Cu** and 14 for **4-Ni**.

According to absorption spectra of **4-H** (Fig. 8), corresponding pegylated phthalocyanine was found both aggregated and nonaggregated in the six solvents that used. This compound has high aggregation tendency in methanol (pink), ethanol (cyan) and aqueous (bright green) solutions. This aggregation species is a sign of H type aggregation formation in these solutions. This formation is easily recognized from blue shift and broadening of their Q band absorption peak [40, 41] in the polar protic solvent solutions. On the other hand, this compound was found as monomeric species in chloroform, dimethylformamide and dimethylsulfoxide solutions.

According to absorption spectra of **4-Co** (Fig. 9), corresponding pegylated phthalocyanine was found disaggregated in all solutions except in the aqueous solution (bright green).

According to absorption spectra of **4-Cu** (Fig. 10), corresponding pegylated phthalocyanine was found aggregated in polar protic solvent solutions similar to **4-H**. It was found that the compound disaggregated in polar aprotic solvent solutions.

Aggregation behavior of compound **4-Ni** is similar to both **4-H** and **4-Cu** according to Fig. 11. While polar protic solvents were increasing the aggregation, polar aprotic solvents decrease the aggregation formation of the phthalocyanine.

Lastly, the aggregation behavior of **4-Zn** is slightly different from the others. It was found highly aggregated only in aqueous solution. But, in the other solutions, it was found disaggregated. In methanol (pink), the peak corresponding to the monomer is still present in the UV-Vis spectrum (Fig.12), besides that, a broadening is seen at blue shift side in the same curve for methanol.

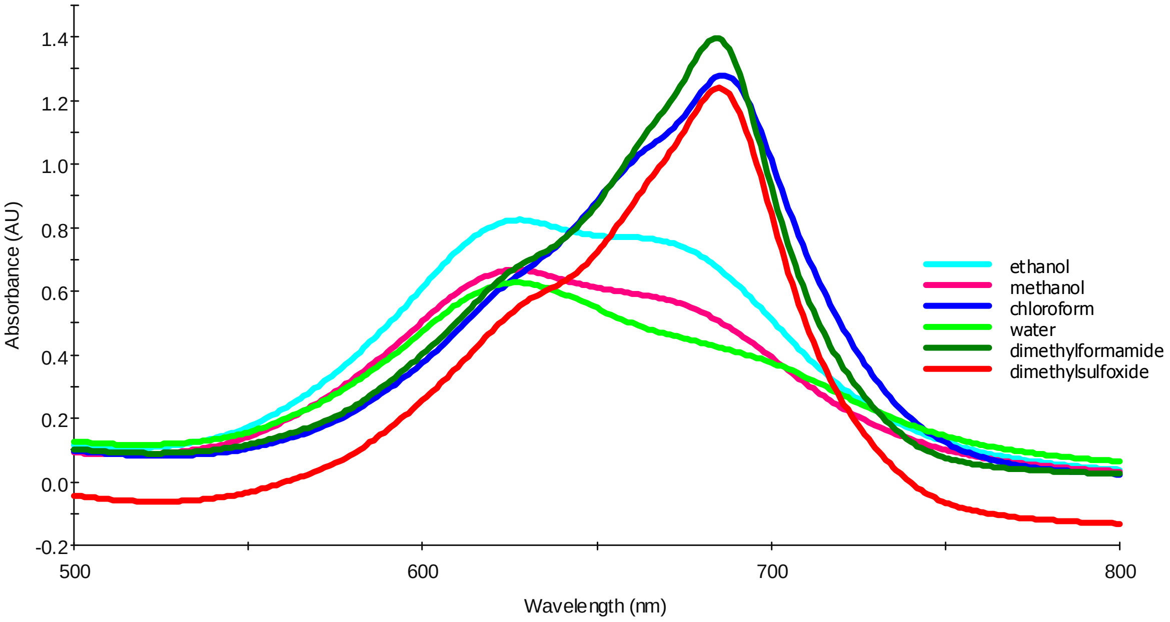


Fig. 8. UV-Vis spectra of **4-H** in different solvents at 3 x10^{-5} M concentration.

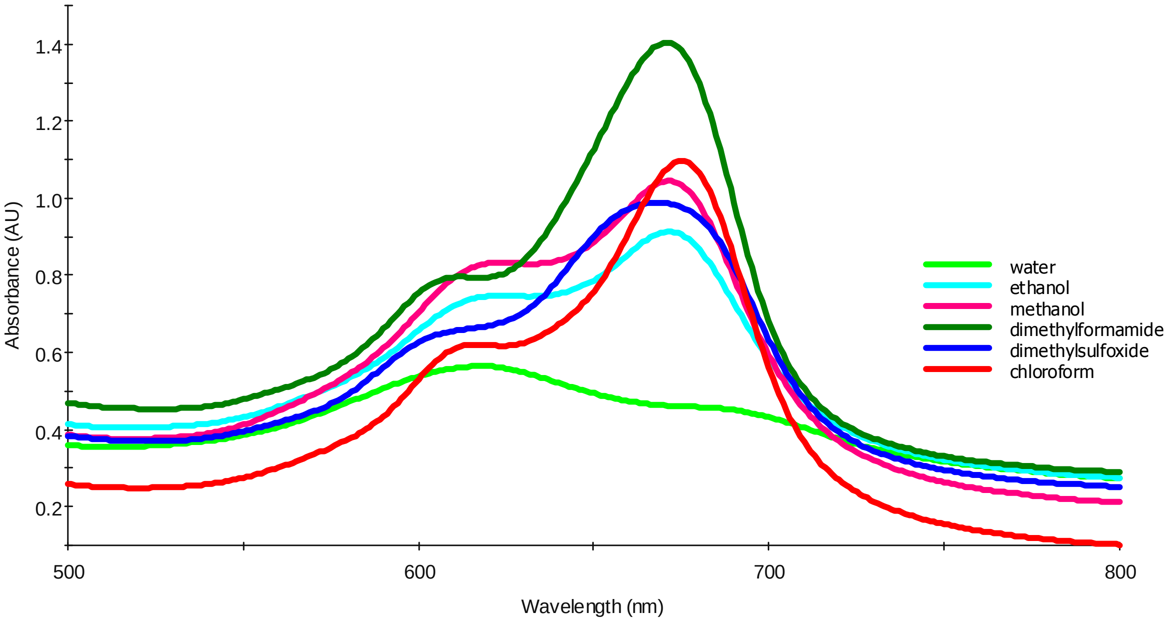


Fig. 9. UV-Vis spectra of **4-Co** in different solvents at 5 x10^{-5} M concentration.

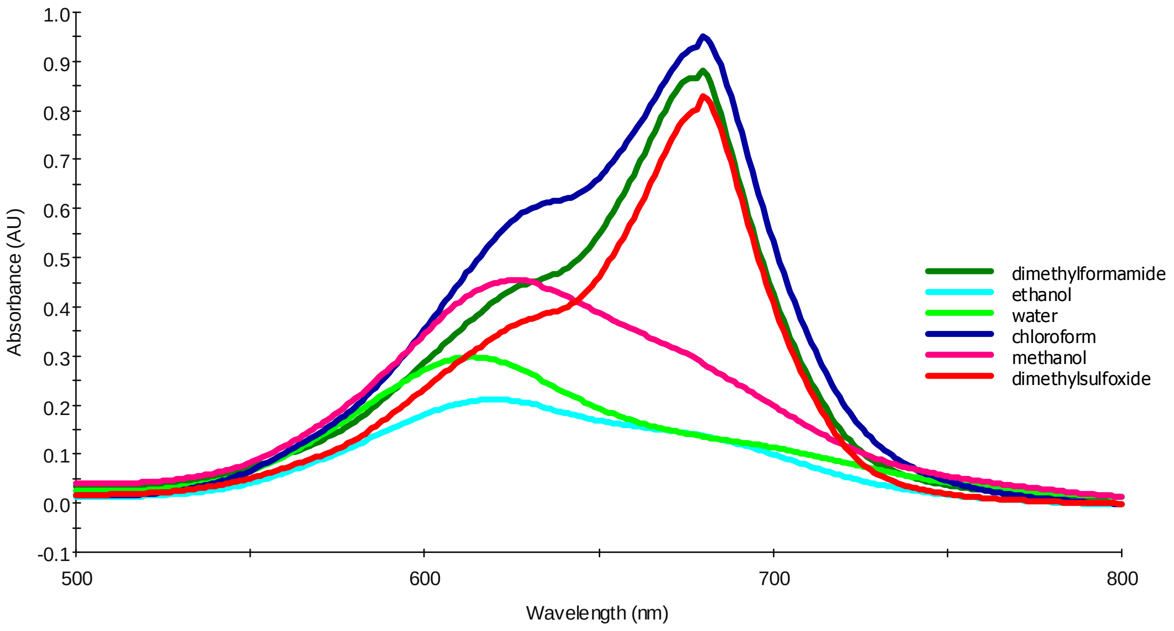


Fig. 10. UV-Vis spectra of **4-Cu** in different solvents at 1 x10^{-5} M concentration.

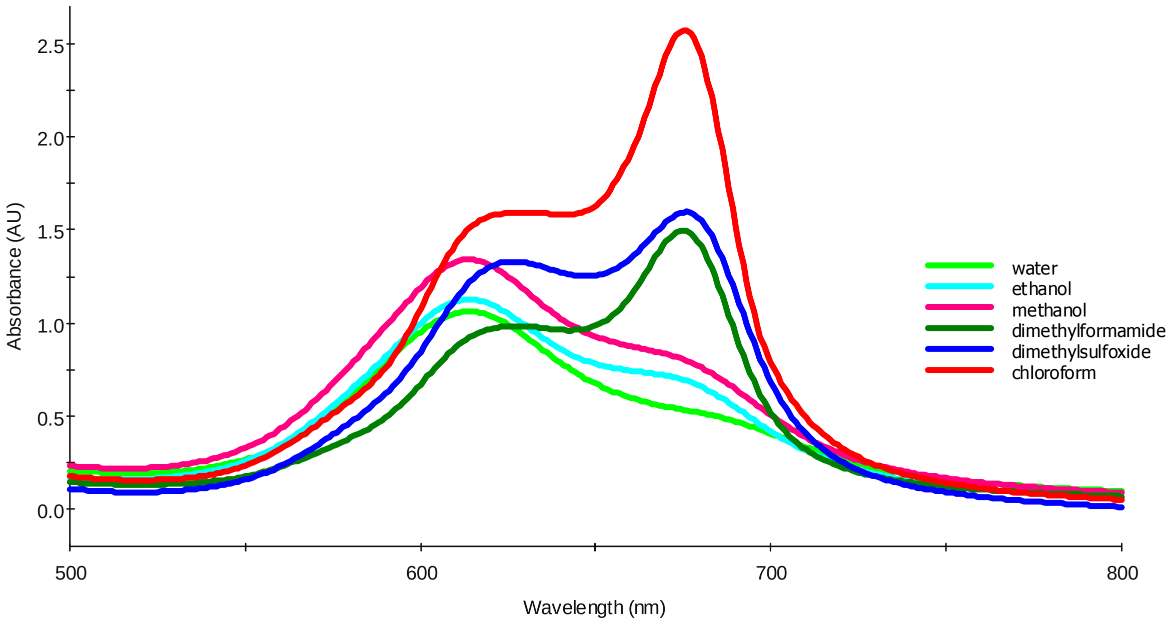


Fig. 11. UV-Vis spectra of **4-Ni** in different solvents at 6.5 x 10^{-5} M concentration.

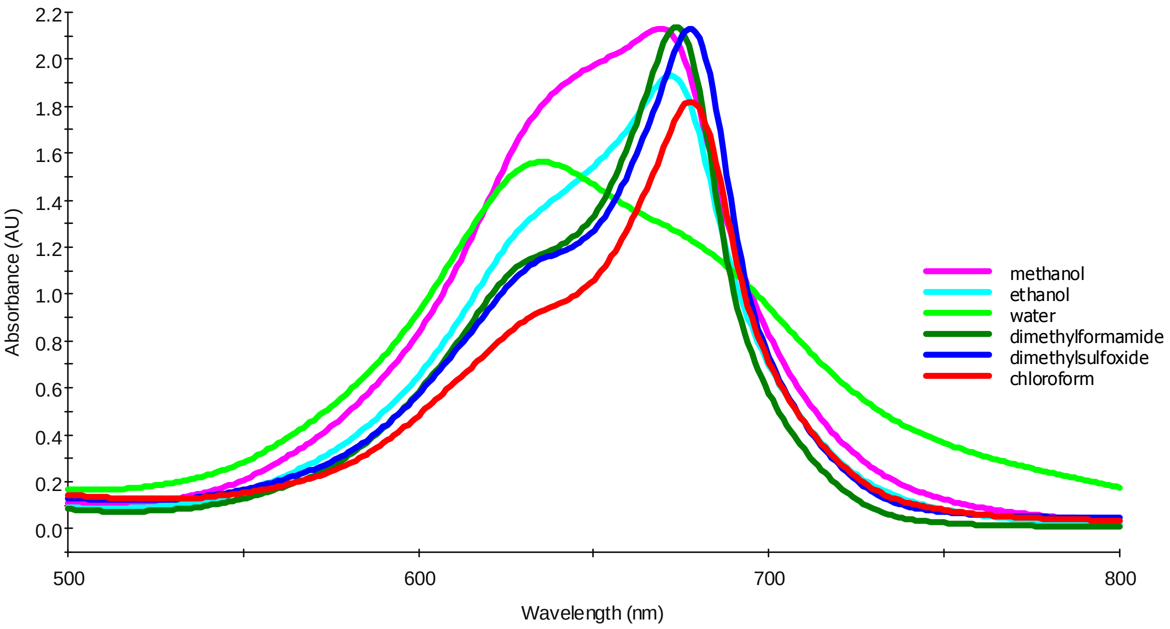
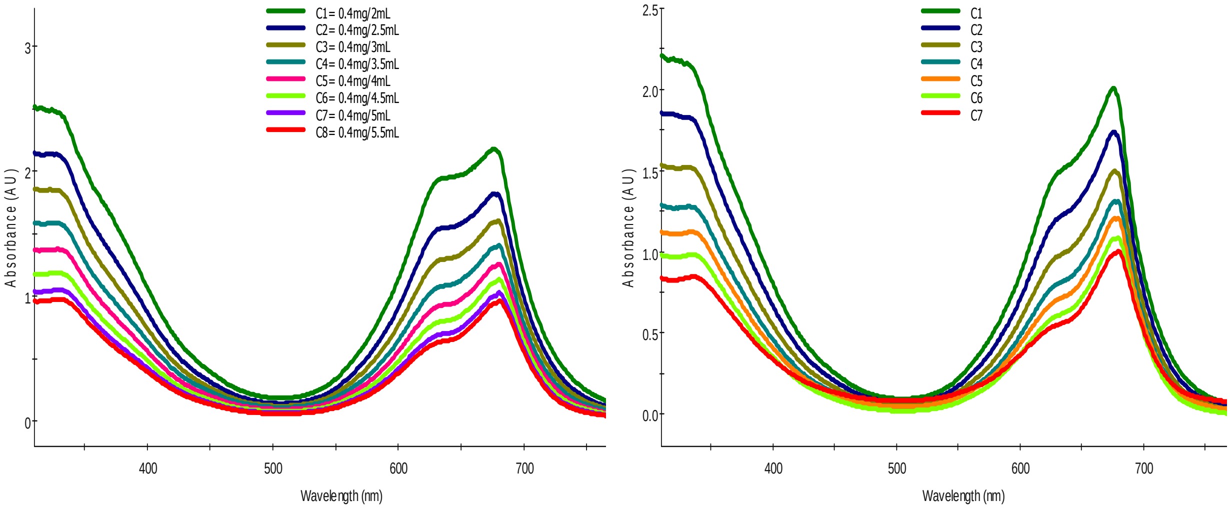


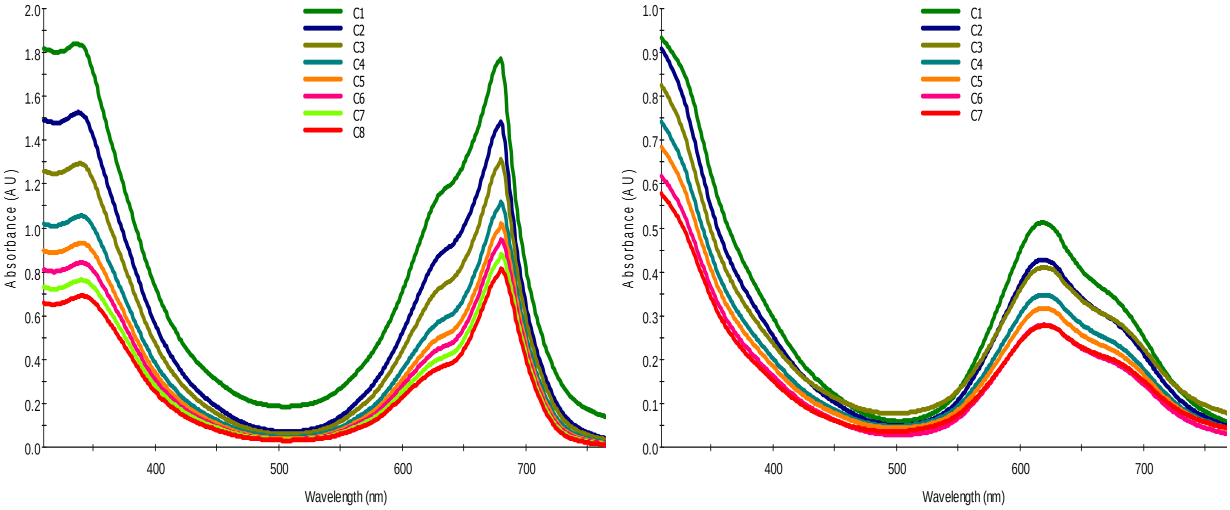
Fig. 12. UV-Vis spectra of **4-Zn** in different solvents at 7 x 10^{-5} M concentration.

Fig. 13 shows dependence on the concentration of the aggregation for **4-Cu**. All spectra were measured at concentrations changing from 9.75x 10^{-5} to 3.5x 10^{-5} M as average eight different concentrations. In the related spectra, it wasn't seen any differentiation from previous studies. Compound **4-Cu** showed disaggregation in chloroform, dimethylformamide and dimethylsulfoxide and aggregation in methanol, ethanol, and water similar to previous studies.



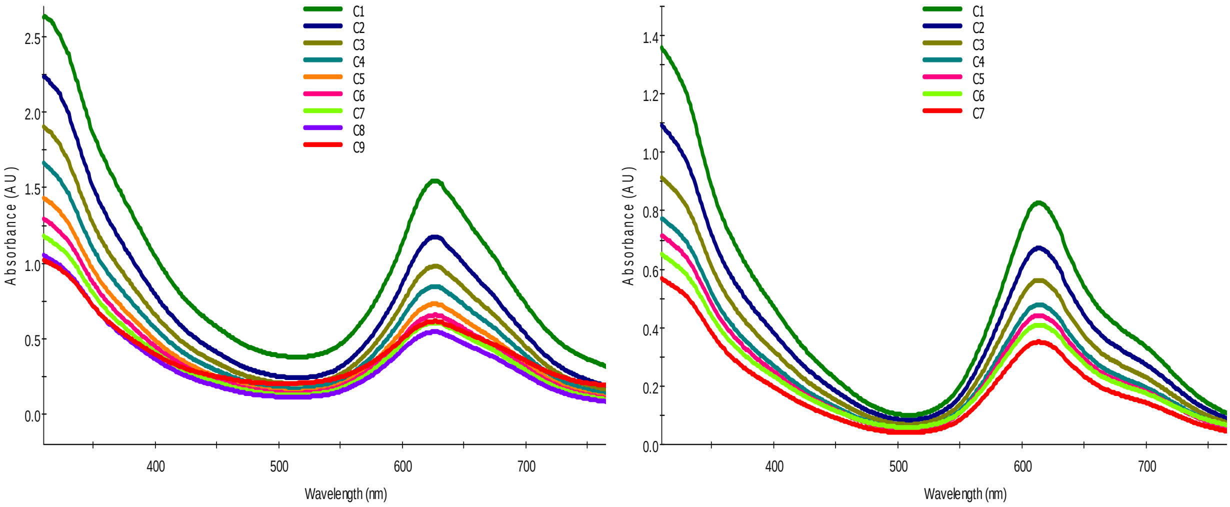
Chloroform

Dimethylformamide



Dimethylsulfoxide

Ethanol

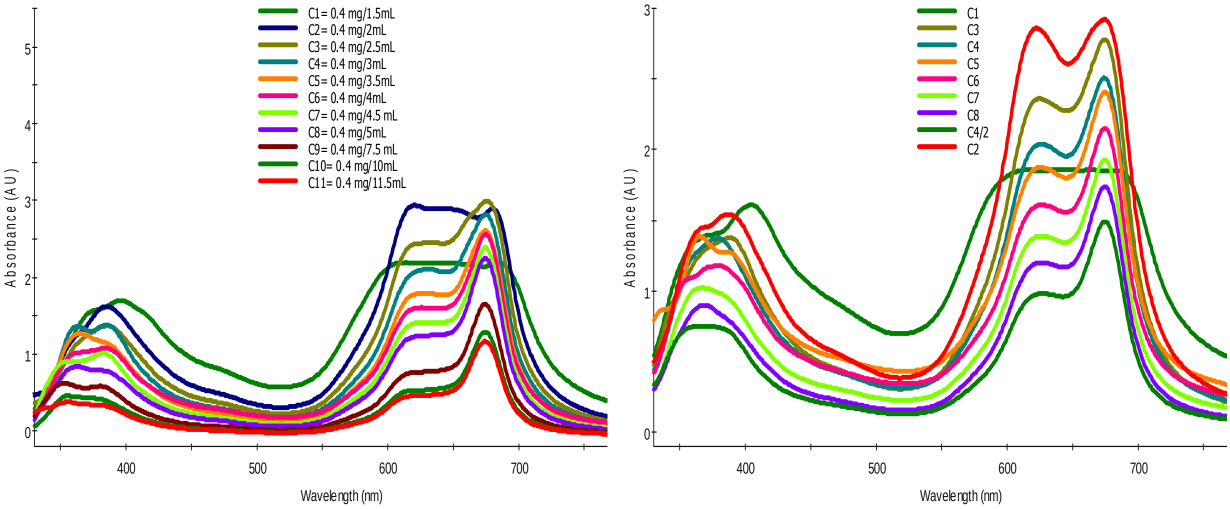


Methanol

Water

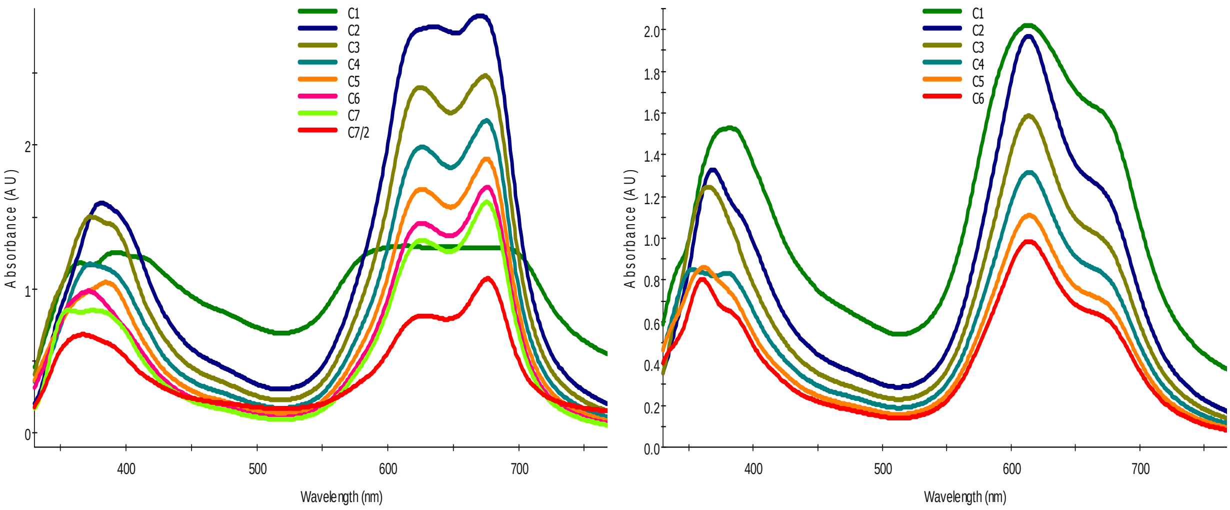
Fig. 13. UV-Vis absorption spectra of **4-Cu** in different solvents at varying concentrations from 9.75 x 10^{-5} M to 3.5 x 10^{-5} M.

Fig. 14 shows dependence on the concentration of the aggregation for **4-Ni**. All spectra were measured at concentrations changing from 1.70 x 10^{-5} to 1.5x 10^{-4} M as average eight different concentrations. These spectra show a differentiation from the others at C1 and C2 concentration, 1.5x 10^{-4} and 9.7 x10^{-5} M, respectively, in polar aprotic solvents. In the former concentration, it is seen that there is a dramatic decline at absorption peak together with the flattening and an alteration at characteristic absorption peak for the Q band of metalled phthalocyanines. As the concentration was decreased to the levels lower than C2, it is seen that there is normalization to the characteristic absorption curves of disaggregated metalled phthalocyanines. In the latter concentration, the absorption curve of **4-Ni** seems as if it belongs to metal free phthalocyanine. It is more suitable to investigate this compound in the concentration lower than 10^{-4} M. In the case of polar protic solvents (methanol, ethanol, and water) it was already seen absorption peak particular to the aggregated status of phthalocyanine in all studied concentrations.



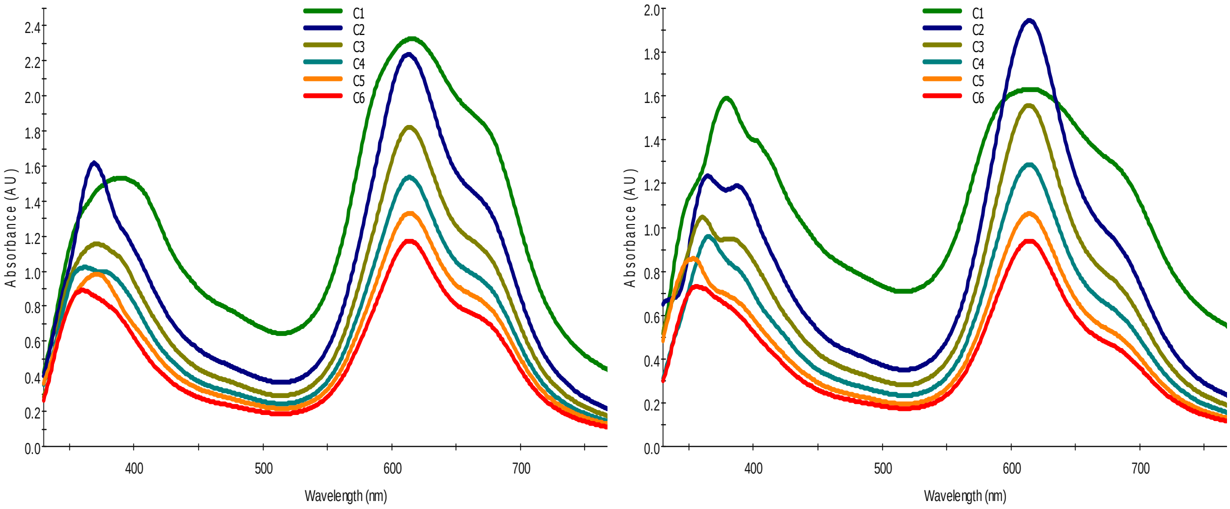
Chloroform

Dimethylformamide



Dimethylsulfoxide

Ethanol



Methanol

Water

Fig. 14. UV-Vis absorption spectra of **4-Ni** in different concentration at varying concentrations from 1.3×10^{-4} M to 1.7×10^{-5} M.

3.3. Thermal decomposition studies

All thermal analysis experiments were carried out in a dry air atmosphere, at 50 mL/min the purge gas flow rate and 20 °C/min heating rate, between 20 °C and 1000 °C by using DTG 60/60H TG/DTA simultaneous measuring instrument. All samples were dried at 120 °C before analysis.

All pegylated phthalocyanines were decomposed at two steps. The first step is related to degradation of PEG chains which are bonded to the phthalocyanine macrocyclic. The second step is related to degradation of the phthalocyanine ring. Onset decomposition temperature of PEG chain in the molecule is 291 °C as a minimum value and offset decomposition temperature of PEG chain is 399 °C as a maximum value in all synthesized phthalocyanine derivatives. Onset and offset decomposition temperatures as the minimum and maximum values of the phthalocyanine ring are 446 °C and 665 °C, respectively. TGA and DTA curves of **4-Cu** as a sample have been given in Fig.15. All the curves for five phthalocyanine compounds are similar to each other with small degradation temperature differences within the ranges given above. Table 1 gives the information about thermal gravimetric analysis results containing decomposition ranges for PEG and Pc rings in the pegylated phthalocyanines.

	Decomposition range temperature (°C)	
Compound code	for PEG	for Pc ring
4-H	304-385	555-665
4-Co	302-382	526-636
4-Cu	319-399	446-605
4-Ni	291-386	511-634
4-Zn	290-391	509-621

Table 1. Thermal analysis results of synthesized phthalocyanines

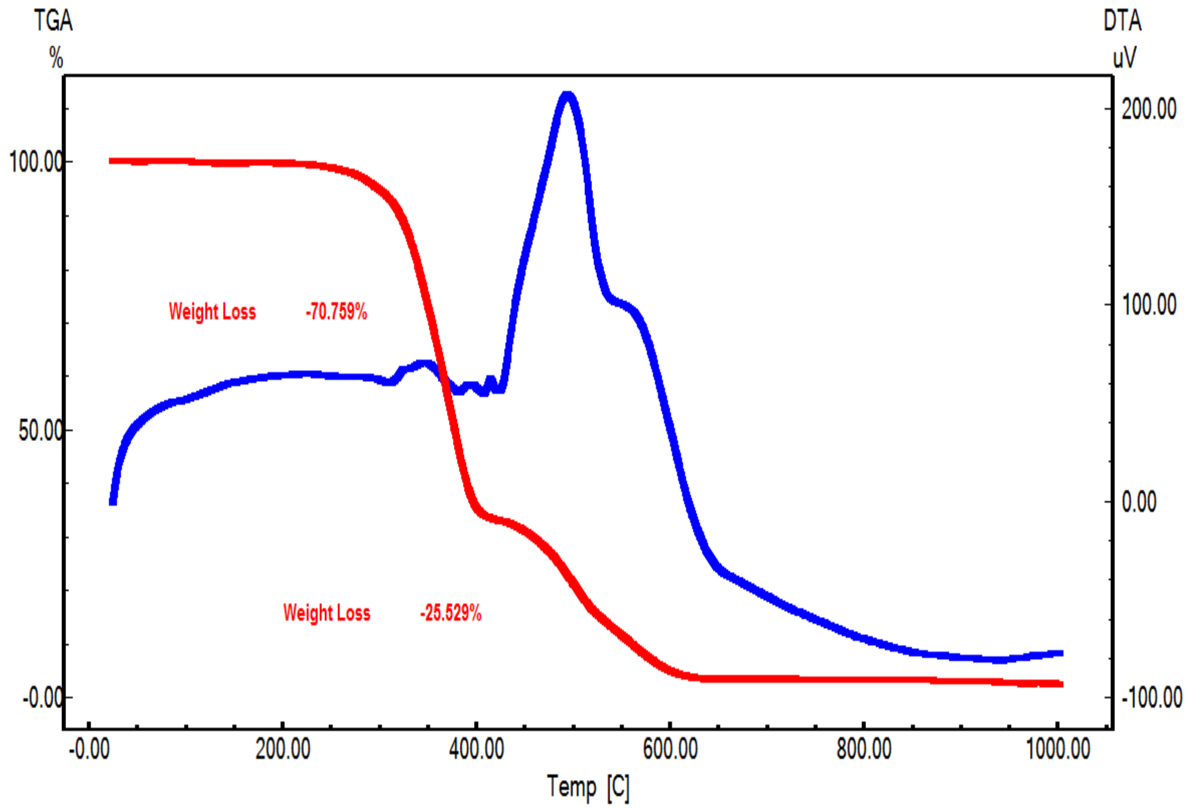


Fig. 15. TGA (red) and DTA (blue) curves of **4-Cu**.

Conclusions

In this paper, we have reported the synthesis and analysis, aggregation status, thermal decomposition ranges of the pegylated phthalocyanine series (symbolized as **4-H, 4-Co, 4-Cu, 4-Ni, and 4-Zn**). Structural analysis of the phthalocyanines and phthalocyanine precursor molecule (symbolized as **4**) were carried on using classical analysis methods such as FTIR, ^{1}H-NMR, ^{13}C NMR, UV-Vis, and elemental analysis. The data confirmed the formation and the structure of targeted molecules. All phthalocyanines have high solubility in water, methanol, ethanol, acetone, pyridine, 1,4-dioxane, dichloromethane, chloroform, tetrahydrofuran, dimethyformamide and dimethylsulfoxide. The phthalocyanines are insoluble in diethyl ether, acetonitrile, hexane and ethyl acetate. Aggregation status of all pegylated phthalocyanines were determined by electronic absorption spectroscopy method. The phthalocyanines were found the aggregated state in polar protic solvent solutions (methanol, ethanol, water) and nonaggregated state in polar aprotic solvent solutions (dimethylformamide, dimethylsulfoxide and chloroform). It was found that there is a small aberration from this state in **4-Co** and **4-Zn**. They showed aggregation only in their aqueous solutions. Thermal degradation temperatures of the phthalocyanines were found at 291 °C minimum value and 665 °C maximum value.

Declaration of interest

Both authors affirm no conflict of interest. The authors are only responsible for the content and writing of this article.

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Highlights

- Tetrasubstituted metalled and metal free phthalocyanines including PEG 400 were synthesized.
- The phthalocyanines were characterized by FTIR, ^{1}H-NMR, ^{13}C NMR, UV-Vis spectroscopies and elemental analysis technique.
- Aggregation statuses of the phthalocyanines were determined depend on the solvents including methanol, ethanol, water, dimethylformamide, dimethylsulfoxide, and chloroform.
- Thermal decomposition ranges of these compounds were determined.