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Photophysical and photochemical properties and comparison of tolyl and tosyl coumarin-bearing phthalocyanines

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ABSTRACT

In this study, peripheral and non-peripherally substituted Zn(II) phthalocyanine complexes were synthesized from 7–hydroxy-3-(*p*-tolyl)coumarin and 7–hydroxy-3-(*p*-tosyl)coumarin compounds. The synthesized new compounds were characterized using elemental analysis, FT-IR, UV–Vis, Fluorescence ^{1}HNMR spectroscopy and MALDI-TOF mass spectrometry. All the synthesized phthalocyanine complexes showed good solubility in organic solvents such as acetone, dichloromethane, chloroform, pyridine, and ethyl acetate. Fluorescent quenching behavior was investigated using 1,4-benzoquinone and potassium iodide as a quencher. The photophysical (fluorescent quantum yields and lifetimes) and photochemical (single oxygen and photodegradation quantum yields) properties of these new phthalocyanines were examined in dimethyl sulfoxide. Phthalocyanine complexes containing 7–hydroxy-3-(*p*-tolyl)coumarin had higher singlet oxygen quantum yields than phthalocyanine complexes containing 7–hydroxy-3-(*p*-tosyl)coumarin. Phthalocyanines to which coumarins are peripherally bound were more advantageous than their non-peripherally bound derivatives. As a result of their photophysical and photochemical properties, coumarin-phthalocyanine complexes containing tolyl-/tosyl- groups can be used as photosensitizing candidates in photodynamic therapy and can be developed with targeted modifications.

1. Introduction

Phthalocyanines (Pc), as second-generation photosensitizers, have been recognized as promising photosensitizers in photodynamic therapy (PDT) research of cancer [1,2]. Due to their easy design, nontoxic properties, and strong absorption between 600 and 800 nm, they create a good therapeutic window and can be preferred as photosensitizers in photodynamic therapy applications [3–6]. In addition to the use of phthalocyanines in photodynamic therapy as a photosensitizer, they have also been investigated in many biological studies for multi-target pharmacology and effective results have been obtained [7–11]. Phthalocyanines have gained great importance in photodynamic therapy with the discovery that the produced singlet oxygen has an important function as a photosensitizer on cancer cells. The photodynamic therapy properties of these compounds can be improved with diamagnetic metal ions such as Zn^{2+}, In^{3+}, Ga^{3+} and Si^{4+} to be found in the cavity of the phthalocyanine core because diamagnetic metals promote intersystem crossing (ISC) [12,13]. In addition, the photophysical and photochemical properties of the cyclic structure can be adjusted as desired by substituting functional groups in various numbers and properties in the peripheral and non-peripheral positions of the cyclic structure [14].

Phthalocyanines are preferred as photosensitizers because of their targeted designability, high singlet oxygen production, low dark toxicity, absorption in the red/infrared region and high molar absorption coefficient [15,16]. A disadvantage is the low solubility and aggregation tendency of phthalocyanines and ways to eliminate this disadvantage have been explored over the years [17]. Phthalocyanine compounds designed with closed-shell diamagnetic ions such as metal cations such as Zn^{2+} are shown as good candidates for photodynamic therapy due to their high triple-state quantum yield and long lifetime [18–20]. To improve the solubility of phthalocyanines in common solvents and reduce their aggregation tendency, high solubility organic groups substituted in the macrocyclic ring are preferred [21,22].

Coumarin and its derivatives represent an important class of oxygenated heterocyclic compounds in chemistry and medicine as lactone ring-containing aromatic-heterocyclic compounds [23]. They are of interest because they can be obtained naturally and are biologically active molecules [24,25]. Coumarins have interesting

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biological properties and are widely available as secondary plant metabolites. It is widely used in medical and biological applications as antibacterial [26,27], antifungal [28,29], antiviral [30,31], antioxidant [32–34], anti-enzymatic [35] and anti-cancer agents [36,37]. Coumarins can be used in medicine by combining them with phthalocyanines, which are effective photosensitizers due to the medical properties of coumarins. It is predicted that coumarins and phthalocyanines will be synthesized by chemical synthesis methods and the resulting complex structure will show similar characteristics.

In this study, Zn(II) phthalocyanine compounds substituted with peripheral and non-peripheral tolyl-/tosyl-coumarin derivatives were investigated. The designed compounds were synthesized and characterized by elemental analysis, UV–Vis, FT-IR, ^{1}HNMR , and MALDI-TOF mass spectroscopy. Photophysical and photochemical properties of these newly synthesized compounds were investigated.

2. Experimental

2.1. Materials and equipment

2.1.1. Materials

All chemicals used were of reagent-grade quality. 2,4-Dihydroxybenzaldehyde, *p*-tolylacetic acid, *p*-toluenesulfonylmethyl isocyanide, 1,3-diphenylisobenzofuran (DPBF), sodium acetate, potassium carbonate, acetic anhydride, and metal salts were purchased from Sigma-Aldrich and used as received. The solvents were purified, dried, and stored over 4 Å molecular sieves. All reactions were carried out under a high-purity N_2 atmosphere unless otherwise noted. The α- and ß- ZnPc compounds (**3**–**6**) were purified successively by washing with hot acetic acid, water, ethanol, and acetonitrile in the Soxhlet apparatus. Column chromatography was performed on silica gel 60 (0.040- 0.063 mm) for proper purification. Melting points of the Pc compounds were found to be higher than 300 °C. The homogeneity of the products was tested in each step by thin-layer chromatography (TLC Silica gel 60 F254).

2.1.2. Equipment

IR spectra were recorded on a Perkin Elmer Spectrum One Fourier transform infrared spectrophotometer. ^{1}HNMR spectra were recorded on a Bruker Avance III 500 MHz Three-channel NMR spectrometer. C, H and N microanalyses were performed on the LECO, CHNS-932 elemental analyzer. Mass spectra were recorded on the Bruker Microflex LT MALDI-TOF Mass Spectrometer equipped with a nitrogen UV-Laser operating at 337 nm using the 2,5-dihydroxybenzoicacid (DHB) and dithranol (DIT) matrix.

Optical spectra in the UV–vis region were recorded with a Shimadzu 2450 UV–vis spectrophotometer. Fluorescence lifetimes were measured using a time-correlated single-photon counting setup (TCSPC) (Horiba Fluorolog 3 equipment.) Fluorescence excitation and emission spectra were recorded on the Hitachi F-7000 spectrofluorometer using a 1 cm path length cuvette at room temperature. Photo irradiations were done using an Osram optic halogen lamp (300W-120 V). 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, and 700 nm with a bandwidth of 40 nm) was additionally placed in the light path before the sample. Light intensities were measured with a POWER MAX PM5100 laser (Molectron detector incorporated) power meter.

2.2. Synthesis and characterization

3-Nitrophthalonitrile and 4-nitrophthalonitrile were synthesized and purified according to the methods described previously in the literature, respectively [38,39]. 7-Hydroxy-3-(*p*-tolyl)coumarin (**1**) and 7–hydroxy-3-(*p*-tosyl)coumarin (**2**) were synthesized with Perkin reaction. 7-(3,4-Dicyanophenoxy)−3-(*p*-tolyl)coumarin (**1a**), 7-(2,3-dicyanophenoxy)−3-(*p*-tolyl)coumarin (**1b**), 7-(3,4-dicyanophenoxy)−3-(*p*-tosyl)coumarin (**2a**), 7-(2,3-dicyanophenoxy)−3-(*p*-tosyl)coumarin (**2b**) were synthesized with nucleophilic aromatic substitution reaction.

2.2.1. 7-Hydroxy-3-(p-tolyl)coumarin (1)

A mixture of 2,4-dihydroxybenzaldehyde 1.84 g (13.30 mmol), *p*-tolylacetic acid 2.00 g (13.30 mmol), sodium acetate 5.46 g (66.00 mmol), and 35 mL anhydrous acetic anhydride was stirred under N_2 atmosphere at 165 °C for 24 h. The reaction mixture was precipitated in 150 mL of ice water and stirred for 24 h, then filtered, and dried. The resulting 7-acetoxy-3-(*p*-tolyl)coumarin was dissolved in methanol and the pH was adjusted to 3 with 10% HCl. Deacetylation was performed by heating at the boiling temperature of 65 °C for 48 h. The final product was filtered, washed with water, and dried. It was purified by recrystallization in ethanol.

7-Hydroxy-3-(*p*-tolyl)coumarin (**1**) is soluble in methanol, ethanol, and tetrahydrofuran. Mp.: 245 °C. Yield: 1.25 g (37.21%). Anal. calculated for $C_{16}H_{12}O_3$: C (76.18%), H (4.79%); found: C (76.19%), H (4.80%). FT-IR (ATR): ν_{max}/cm^{-1}: 3235 (Ar OH), 3070–3030 (Ar C–H), 2913, 2850 (Aliphatic C–H), 1693 (C = O), 1511 (C = C).

2.2.2. 7-Hydroxy-3-(p-tosyl)coumarin (2)

A mixture of 2,4-hydroxybenzaldehyde 1.41 g (10.00 mmol), *p*-toluenesulfonylmethyl isocyanide 2.00 g (10.10 mmol), 2–3 drops of piperidine, and 40 mL dry ethanol was stirred under N_2 atmosphere at 70 °C for 2 h. The resulting imino coumarin was acidified with 10% hydrochloride acid in methanol and heated under reflux at 70 °C for 24 h, and 7–hydroxy-3-(p-tosyl)coumarin was obtained from the hydrolyzed imino coumarin. Methanol was removed from the reaction medium using evaporation. The final product was filtered, washed with water, and dried. It was purified by recrystallization in ethanol.

7-Hydroxy-3-(*p*-tosyl)coumarin (**2**) is soluble in methanol, ethanol, ethyl acetate, dichloromethane, chloroform, tetrahydrofuran and dimethylformamide. Mp.: 232–235 °C. Yield: 2.88 g (88.99%). Anal. calculated for $C_{16}H_{12}O_5S$: C (60.75%), H (3.82%); found: C (60.72%), H (3.84%). FT-IR (ATR): ν_{max}/cm^{-1}: 3524 (Ar, OH), 3067–3030 (Ar, C–H), 2924, 2853 (Alifatic, C–H), 1715 (C = O), 1557 (C = C), 1321–1165 (R_2SO_2).

2.2.3. 7-(3,4-Dicyanophenoxy)−3-(p-tolyl)coumarin (1a)

Mixture of 7–hydroxy-3-(*p*-methylphenyl)coumarin 1.13 g (4.50 mmol), 4-nitrophthalonitrile 0.78 (4.50 mmol), potassium carbonate 0.93 g (6.70 mmol), and 30 mL of dry dimethylformamide in a one-necked flask, under N_2 atmosphere, was stirred at 50 °C for five days. The reaction mixture was acidified with a dilute solution of hydrochloric acid in ice water. The precipitated product was washed with water until neutral and dried. The obtained product was purified by the column chromatography method in dichloromethane/hexane (10:1) mixture.

7-(3,4-Dicyanophenoxy)−3-(*p*-tolyl)coumarin (**1a**) is soluble in ethyl acetate, dichloromethane, chloroform, tetrahydrofuran, and *N,N*-dimethylformamide. Mp.: 184–187 °C. Yield: 1.28 g (73.41%). Anal. calculated for $C_{24}H_{14}N_2O_3$: C (76.18%), H (3.73%), N (7.40%); found: C (76.19%), H (3.74%), N (7.39%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 334 (5.27). FT-IR (ATR): ν_{max}/cm^{-1}: 3077–3036 (Ar, C–H), 2918, 2857 (Aliphatic, C–H), 2232 (C≡N), 1729 (C = O), 1593 (C = C), 1257 (Ar–O–Ar). ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.81 (d, J = 7.13 Hz, 1H), 7.61 (d, J = 8.70 Hz, 2H), 7.60 (d, J = 8.90 Hz, 1H), 7.40 (d, J = 2.45 Hz, 1H), 7.36 (dd, J = 8.70

and 2.52 Hz, 1H), 7.28 (d, J = 8.47 Hz, 2H), 7.08 (d, J = 2.29 Hz, 1H), 7.01 (dd, J = 8.47 and 2.47 Hz, 1H), 2.41 (s, 3H).

*2.2.4. 7-(2,3-Dicyanophenoxy)−3-(*p*-tolyl)coumarin (1b)*

7-Hydroxy-3-(*p*-methylphenyl)coumarin 0.75 g (2.90 mmol), 3-nitrophthalonitrile 0.53 g (2.90 mmol), potassium carbonate 0.62 g (4.39 mmol), and 25 mL of dry dimethylformamide mixture was mixed with a magnetic stirrer in a single-necked flask in N_2 atmosphere at 50 °C for seven days. The reaction mixture was acidified with a dilute solution of hydrochloric acid in ice water. The precipitated product was washed with water until neutral and dried. The obtained product was purified by the column chromatography method in dichloromethane/hexane (10:1) mixture.

7-(2,3-Dicyanophenoxy)−3-(*p*-tolyl)coumarin (**1b**) is soluble in ethyl acetate, dichloromethane, chloroform, tetrahydrofuran, and *N,N*-dimethylformamide. Mp.: 234.5 °C. Yield: 1.00 g (83.16%). Anal. calculated for $C_{24}H_{14}N_2O_3$: C (76.18%), H (3.73%), N (7.40%); found: C (76.21%), H (3.72%), N (7.41%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 334 (5.31). FT-IR (ATR): ν_{max}/cm^{-1}: 3095–3035 (Ar, C–H), 2919, 2956 (Aliphatic, C–H), 2231 (C≡N), 1716 (C = O), 1587 (C = C), 1280 (Ar –O–Ar). ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.70 (dd, J = 7.90 and 7.80 Hz, 1H), 7.66 (d, J = 8.19 Hz, 1H), 7.61 (dd, J = 9.00 and 2.56 Hz, 1H), 7.60 (dd, J = 9.00 and 2.56 Hz, 1H), 7.53 (d, J = 8.01 Hz, 2H), 7.51 (d, J = 8.01 Hz, 2H), 7.27 (d, J = 8.51 Hz, 1H), 7.05 (s, 1H), 2.35 (s, 3H).

2.2.5. 7-(3,4-Dicyanophenoxy)−3-(p-tosyl)coumarin (2a)

Mixture of 7–hydroxy-3-(*p*-tosyl)coumarin 1.50 g (4.00 mmol), 4-nitrophthalonitrile 0.71 g (4.00 mmol), potassium carbonate 0.98 g (7.00 mmol) and 35 mL dry dimethylformamide in a single-necked flask, in N_2 atmosphere, was mixed with a magnetic stirrer for twelve days at 50 °C. The reaction mixture was acidified with a dilute solution of hydrochloric acid in ice water. The precipitated product was washed with water until neutral and dried. The obtained product was purified by the column chromatography method in dichloromethane/hexane (10:1) mixture.

7-(3,4-Dicyanophenoxy)−3-(*p*-tosyl)coumarin (**2a**) is soluble in ethyl acetate, dichloromethane, chloroform, tetrahydrofuran, and *N,N*-dimethylformamide. Mp.: 135–137 °C. Yield: 0.83 g (40.09%). Anal. calculated for $C_{24}H_{14}N_2O_5S$: C (65.15%), H (3.19%), N (6.33%); found: C (65.18%), H (3.20%), N (6.31%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 291 (5.01). FT-IR (ATR): ν_{max}/cm^{-1}: 3074–3037 (Ar, C–H), 2924, 2853 (Aliphatic, C–H), 2232 (C≡N), 1726 (C = O), 1560 (C = C), 1255 (Ar–O–Ar), 1320 and 1168 (R_2SO_2). ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.71 Hz, 1H), 7.77 (s, 1H), 7.76 (d, J = 8.75 Hz, 2H), 7.75 (br s, 1H), 7.68 (d, J = 8.19 Hz, 1H), 7.31 (d, J = 7.96 Hz, 1H), 7.22 (d, J = 2.49 Hz, 1H), 7.01 (dd, J = 8.59 and 2.32 Hz, 1H), 6.94 (d, J = 8.70 Hz, 2H), 2.47 (s, 3H).

*2.2.6. 7-(2,3-Dicyanophenoxy)−3-(*p*-tosyl)coumarin (2b)*

Mixture of 7–hydroxy-3-(*p*-tosyl) coumarin 0.75 g (2.30 mmol), 3-nitrophthalonitrile 0.41 g (2.30 mmol), potassium carbonate 0.49 g (3.40 mmol) and 25 mL of dry dimethylformamide in a single-necked flask, in N_2 atmosphere, it was mixed with a magnetic stirrer for ten days at 50 °C. The reaction mixture was acidified with a dilute solution of hydrochloric acid in ice water. The precipitated product was washed with water until neutral and dried. The obtained product was purified by the column chromatography method in dichloromethane/hexane (10:1) mixture.

7-(2,3-Dicyanophenoxy)−3-(*p*-tosyl) coumarin (**2b**) is soluble in ethyl acetate, dichloromethane, chloroform, tetrahydrofuran, and *N,N*-dimethylformamide. Mp.: 135–138 °C. Yield: 0.36 g (34.48%). Anal. calculated for $C_{24}H_{14}N_2O_5S$: C (65.15%), H (3.19%), N (6.33%); found: C (65.17%), H (3.21%), N (6.32%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 288 (5.18). FT-IR (ATR): ν_{max}/cm^{-1}: 3085–3051 (Ar, C–H), 2930, 2859 (Aliphatic, C–H), 2233 (C≡N), 1721 (C = O), 1550 (C = C), 1255 (Ar–O–Ar), 1350 and 1143 (R_2SO_2). ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 8.18 Hz, 1H), 7.71 (s, 1H), 7.67 (dd, J = 8.45 and 7.76 Hz, 1H), 7.58 (d, J = 7.75 Hz, 1H), 7.35 (d, J = 7.84 Hz, 2H), 7.25 (d, J = 7.84 Hz, 2H), 7.15 (d, J = 8.59 Hz, 1H), 6.94 (dd, J = 8.60 and 2.35 Hz, 1H), 6.68 (d, J = 2.32 Hz, 1H), 2.46 (s, 3H).

*2.2.7. 2,9(10),16(17),23(24)-Tetrakis[7-oxo-3-(*p*-tolyl)coumarin] zinc(II) phthalocyanine (3)*

Mixture of 7-(3,4-dicyanophenoxy)−3-(*p*-tolyl)coumarin (**1a**) 0.18 g (0.48 mmol), $Zn(OAc)_2{\cdot}2H_2O$ 0.02 g (0.12 mmol), and 3 mL of 2-*N,N*-dimethylaminoethanol in N_2 atmosphere was stirred with a magnetic stirrer at 165 °C for one day. After the reaction mixture was cooled to room temperature, it was precipitated in ice water, then filtered. The obtained green precipitate was washed with dilute acetic acid, water, methanol, acetone, ether, and ethyl acetate and then dried.

Compound **3** is soluble in dichloromethane, tetrahydrofuran, dimethyl sulfoxide and *N,N*-dimethylformamide. Mp.: >300 °C. Yield: 0.03 g (15.78%). Anal. calculated for $C_{96}H_{56}N_8O_{12}Zn$: C (73.03%), H (3.58%), N (7.10%); found: C (73.01%), H (3.57%), N (7.10%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 342 (5.00), 605 (3.38), 671 (5.09). FT-IR (ATR): ν_{max}/cm^{-1}: 3070–3030 (Ar, C–H), 2925, 2862 (Aliphatic, C–H), 1725 (C = O), 1563 (C = C), 1264 (Ar–O–Ar). MALDI-TOF-MS *m/z*: Calc. 1580.073 $[M]^+$; found 1581.074 $[M + H]^+$.

*2.2.8. 1,8(11),15(18),22(25)-Tetrakis[7-oxo-3-(*p*-tolyl)coumarin] zinc(II) phthalocyanine (4)*

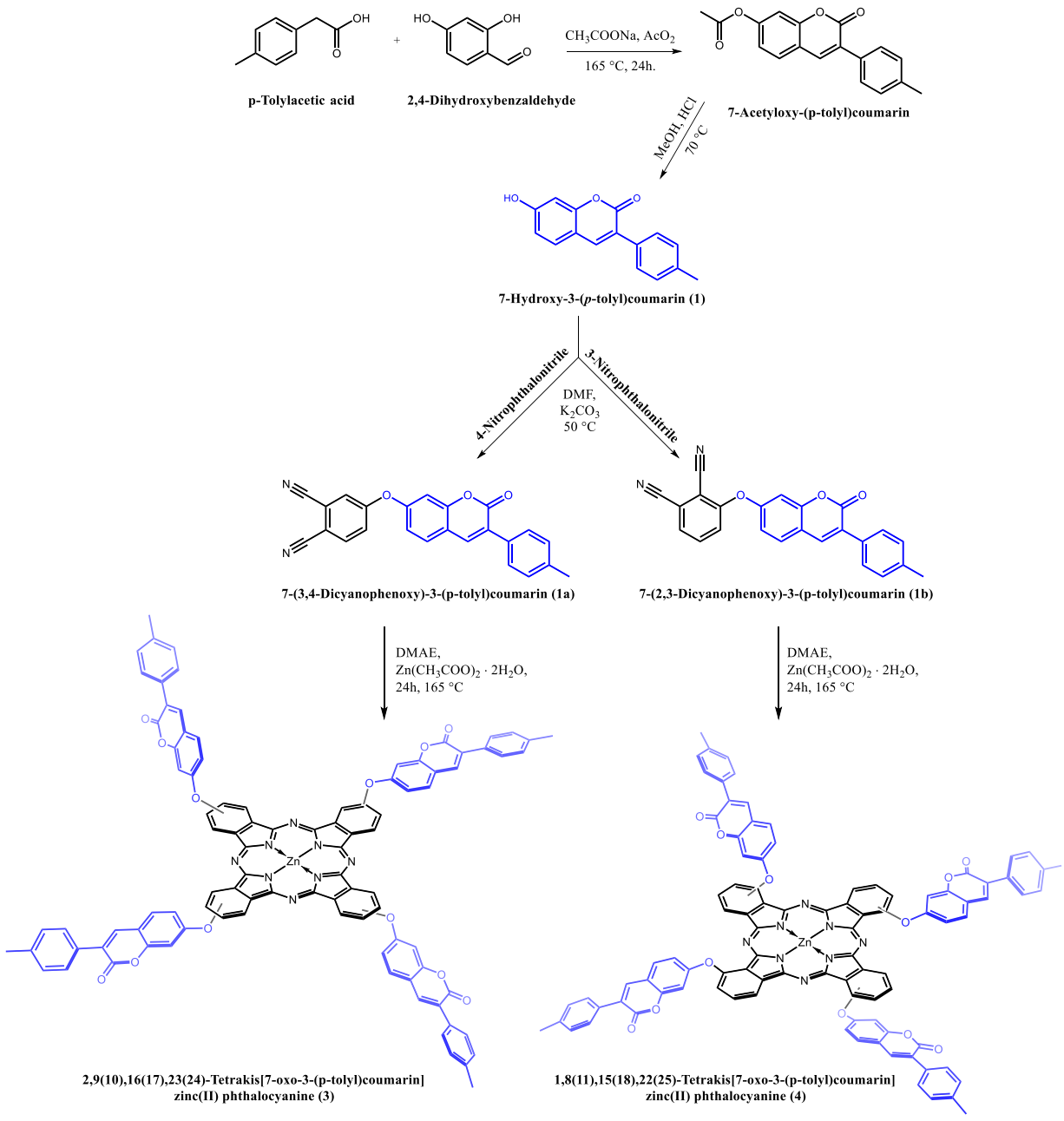
Mixture of 7-(2,3-diyanophenoxy)−3-(*p*-tolyl)coumarin (**1b**) 0.15 g (0.40 mmol), $Zn(OAc)_2{\cdot}2H_2O$ 0.02 g (0.01 mmol) and 3 mL of *N,N*-dimethylaminoethanol under N_2 atmosphere was stirred with a magnetic stirrer at 165 °C for one day. After the reaction mixture was cooled to room temperature, it was poured into water, The obtained green precipitate was washed with dilute acetic acid, water, methanol, acetone, ether, and ethyl acetate, and dried.

Compound **4** is soluble in dichloromethane, tetrahydrofuran, dimethyl sulfoxide and *N,N*-dimethylformamide. Mp.: >300 °C. Yield: 0.02 g (13%). Anal. calculated for $C_{96}H_{56}N_8O_{12}Zn$: C (73.03%), H (3.58%), N (7.10%); found: C (73.04%), H (3.55%), N (7.11%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 339 (5.07), 619 (4.50), 687 (5.25). FT-IR (ATR): ν_{max}/cm^{-1}: 3064–3022 (Ar, C–H), 2954, 2820 (Aliphatic, C–H), 1717 (C = O), 1581 (C = C), 1263 (Ar–O–Ar). MALDI-TOF-MS *m/z*: Calc. 1579.875; found 1603.154 $[M + H{+}Na]^+$.

*2.2.9. 2,9(10),16(17),23(24)-Tetrakis[7-oxo-3-(*p*-tosyl)coumarin] zinc(II) phthalocyanine (5)*

Mixture of 7-(3,4-dicyanophenoxy)−3-(*p*-tosyl)coumarin (**2a**) 0.10 g (0.22 mmol), $Zn(OAc)_2{\cdot}2H_2O$ 0.10 g (0.05 mmol), and 3 mL of *N,N*-dimethylaminoethanol under N_2 atmosphere was stirred with a magnetic stirrer at 165 °C for 5 h. After the reaction mixture was cooled to room temperature, it was poured into water, and the green product was allowed to precipitate. The final product was washed with dilute acetic acid, water, methanol, acetone, ether, and ethyl acetate and dried.

Compound **5** is soluble in dichloromethane, tetrahydrofuran, dimethyl sulfoxide and *N,N*-dimethylformamide. Mp.: 220–221 °C. Yield: 0.02 g (20%). Anal. calculated for $C_{96}H_{56}N_8O_{20}S_4Zn$: C (62.83%), H (3.08%), N (6.11%); found: C (62.81%), H (3.10%), N (6.12%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 338 (4.75), 610 (4.38), 667 (5.07). FT-IR (ATR): ν_{max}/cm^{-1}: 3060–3039 (Ar, C–H), 2922, 2851 (Aliphatic, C–H), 1716 (C = O), 1550 (C = C), 1258 (Ar–O–Ar), 1360 and 1140 (R_2SO_2). MALDI-TOF-MS *m/z*: Calc. 1835.16; found 1923.75 $[M + H_2O{+}3Na]^+$.



Scheme 1. Synthesis of coumarin **1** and their phthalonitrile (**1a**-**b**) and zinc(II) phthalocyanine derivatives (**3**,**4**).

*2.2.10. 1,8(11),15(18),22(25)-Tetrakis[7-oxo-3-(*p*-tosyl)coumarin] zinc(II) phthalocyanine (6)*

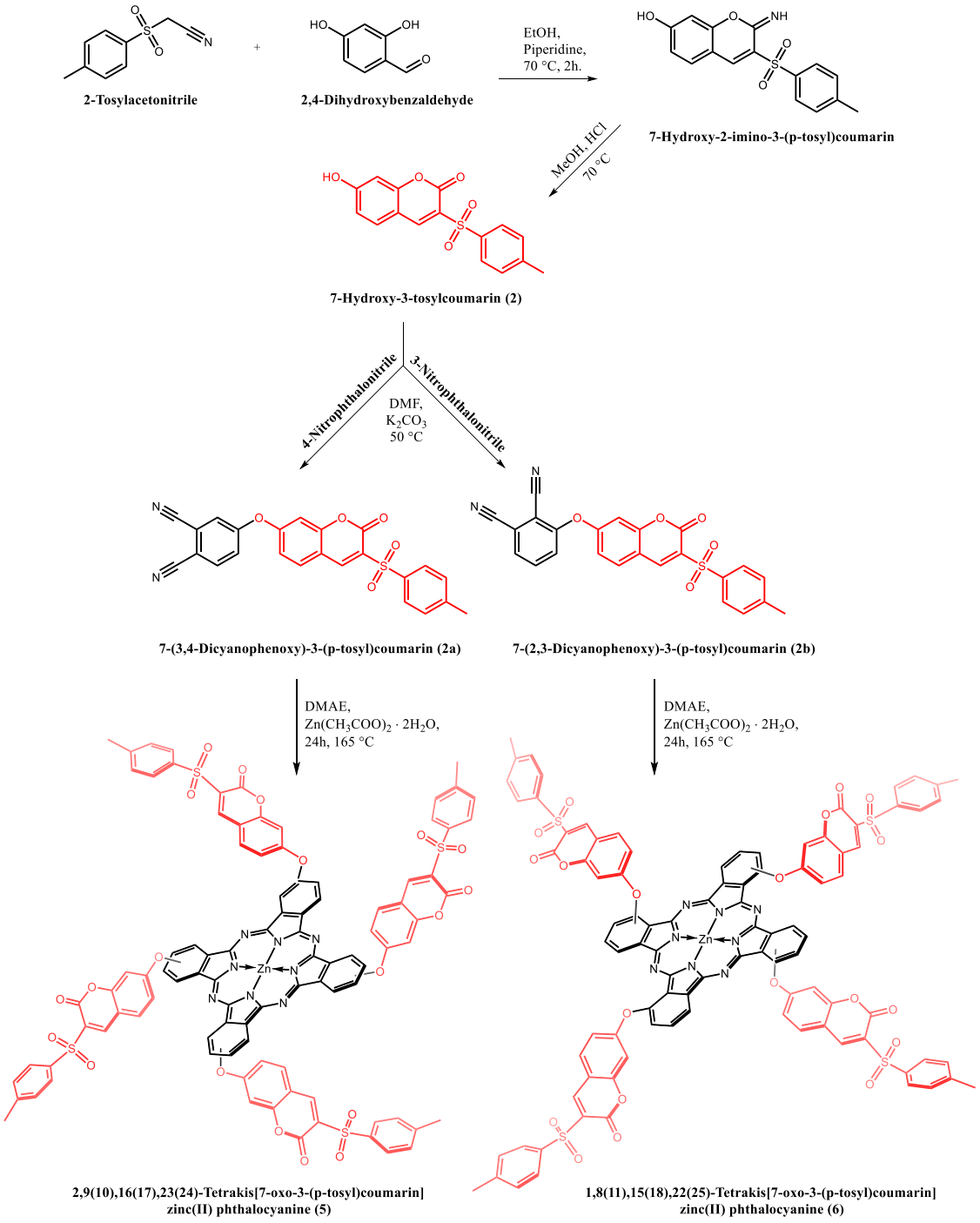
Mixture of 7-(2,3-diyanophenoxy)−3-(*p*-tosyl)coumarin (**2b**) 0.10 g (0.22 mmol), $Zn(OAc)_2{\cdot}2H_2O$ 0.10 g (0.05 mmol), and 1 mL of 2-*N*,*N*-dimethylaminoethanol under N_2 atmosphere was stirred with a magnetic stirrer at 145 °C for 5 h. After the reaction mixture was cooled to room temperature, it was poured into water, and the green product was allowed to precipitate. The obtained product was washed with dilute acetic acid, water, methanol, acetone, ether, and ethyl acetate and dried.

Compound **6** is soluble in dichloromethane, tetrahydrofuran, dimethyl sulfoxide and *N*,*N*-dimethylformamide. Mp.: 220–222 °C. Yield: 0.02 g (18%). Anal. calculated for $C_{96}H_{56}N_8O_{20}S_4Zn$: C (62.83%), H (3.08%), N (6.11%); found: C (62.82%), H (3.07%), N (6.13%). UV–vis, λ_{max} (1×10^{-5} M, in DMSO) nm (logε): 316 (4.59), 625 (4.03), 693 (4.72). FT-IR (ATR): ν_{max}/cm^{-1}: 3082–3057 (Ar, C–H), 2920, 2849 (Aliphatic, C–H), 1726 (C = O), 1550 (C = C), 1328 (Ar–O–Ar), 1358 and 1138 (R_2SO_2). MALDI-TOF-MS *m/z*: Calc. 1835.16; found 1840.72 $[M + 5H]^+$.

3. Result and discussion

The synthesis schemes of peripheral and non-peripheral zinc Pc's containing tolyl- and tosyl-coumarins are shown in Scheme 1 and 2, respectively.

7-Hydroxy-3-(*p*-tolyl)coumarin (**1**) was synthesized by Perkin reaction using p-tolylacetic acid and 2,4-dihydroxybenzaldehyde in the presence of acetic anhydride and sodium acetate at 165 °C. 7-Hydroxy-3-(*p*-tosyl)coumarin (**2**) was synthesized by the Knoevenagel reaction using *p*-tosylacetonitrile and 2,4-dihydroxybenzaldehyde in the presence of ethanol and piperidine at 65 °C. Phthalonitrile derivatives of these two coumarins (**1** and **2**) were synthesized via nucleophilic aromatic substitution reaction



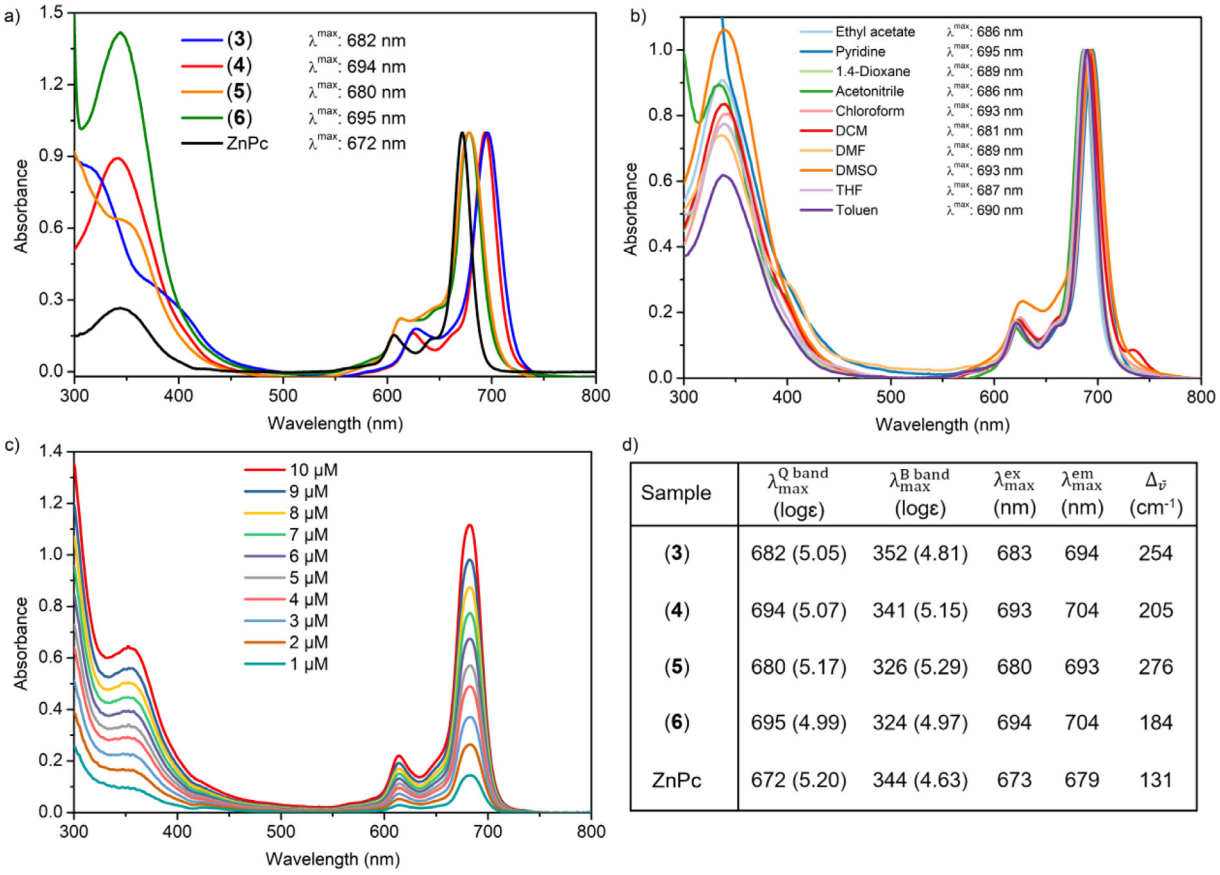
Scheme 2. Synthesis of coumarin **2** and their phthalonitrile (**2a**-**b**) and zinc(II) phthalocyanine derivatives (**5,6**).

using 3-nitrophthalonitrile and 4-nitrophthalonitrile, respectively, in anhydrous *N,N*-dimethylformamide under an N_2 atmosphere.

Peripheral and non-peripheral zinc(II) phthalocyanines were prepared by cyclotetramerization of coumarin-phthalonitrile derivatives. Tolyl-/tosyl-coumarin substituted zinc(II) phthalocyanines were prepared in dry *N,N*-dimethylaminoethanol at 165 °C in the presence of zinc acetate. All obtained products were purified by the column chromatography method.

Generally, unsubstituted phthalocyanine complexes do not dissolve well in organic solvents, but the solubility of phthalocyanines containing polar groups is generally good according to the literature [40–42]. All synthesized zinc phthalocyanines showed excellent solubility in organic solvents such as ethyl acetate, pyridine, 1,4-dioxane, acetonitrile, chloroform, dichloromethane, *N,N*-dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, and toluene.

All newly synthesized compounds were characterized by elemental analysis, FT-IR, UV–vis, ^{1}HNMR , and MALDI-TOF-MS spectroscopy techniques. In the IR spectra of the compounds obtained, the characteristic peak of the lactone carbonyl (–C = O) group on tolyl coumarin was observed at approximately 1693 cm^{-1}. The peak of the hydroxyl (–OH) group in the structure of tolyl coumarin was observed at approximately 3235 cm^{-1}. The characteristic peak of the lactone carbonyl (–C = O) group on tosyl



Sample	$\lambda_{max}^{Q\ band}$ (logε)	$\lambda_{max}^{B\ band}$ (logε)	λ_{max}^{ex} (nm)	λ_{max}^{em} (nm)	$\Delta_{\tilde{\nu}}$ (cm^{-1})
(**3**)	682 (5.05)	352 (4.81)	683	694	254
(**4**)	694 (5.07)	341 (5.15)	693	704	205
(**5**)	680 (5.17)	326 (5.29)	680	693	276
(**6**)	695 (4.99)	324 (4.97)	694	704	184
ZnPc	672 (5.20)	344 (4.63)	673	679	131

Fig. 1. a) The UV–Vis comparison of synthesized phthalocyanines in DMSO. b) UV–Vis comparison of (**4**) in different solvents. c) UV–Vis spectra of (**3**) at ten different concentrations in DMSO. d) UV–Vis and fluorescence data of phthalocyanine compounds (**3**–**6**).

coumarin was observed at approximately 1715 cm^{-1}. Peaks belonging to the hydroxyl (–OH) group in the structure of tosyl coumarin were also observed at approximately 3524 cm^{-1}. The hydroxyl (–OH) peak of coumarins disappeared in the IR spectra of phthalonitrile derivatives. Peaks of –C≡N groups of phthalonitrile derivatives of tolyl coumarin were observed at approximately 2231 and 2232 cm^{-1}, respectively. The peaks of Ar–O–Ar groups of phthalonitrile derivatives of tolyl coumarin were observed at approximately 1280 cm-1 and 1257 cm^{-1}, respectively. Peaks of –C≡N groups of phthalonitrile derivatives of tosyl coumarin were observed at approximately 2233 and 2232 cm^{-1}, respectively. The peaks of the Ar–O–Ar groups of phthalonitrile derivatives of tosyl coumarin are approximate. It was observed at 1255 cm^{-1}. The disappearance of the peaks belonging to this hydroxyl (–OH) group of tolyl and tosyl coumarin phthalonitrile derivatives and the observation of the peaks of the –C≡N and Ar–O–Ar groups indicate the formation of phthalonitrile derivatives. The –C≡N peak, usually seen at 2230 cm^{-1} in phthalonitrile derivatives, was not observed after conversion to phthalocyanines. The disappearance of the –C≡N peaks in all phthalocyanines is evidence of the formation of phthalocyanine compounds (Figures S2 and S7).

When the ^{1}HNMR spectra of phthalonitrile compounds are examined, generally aromatic and alkyl proton peaks for tolyl coumarin phthalonitrile derivatives are between 7.81–7.01 ppm and 2.41–2.35 ppm, respectively. For tosyl coumarin phthalonitrile derivatives, the aromatic and alkyl proton peaks are between 7.80–6.68 ppm and 2.47–2.46 ppm, respectively, and the integrations also fit correctly (Figures S3, S4, S8 and S9).

MALDI-TOF mass spectra are an important characterization technique used to determine the molecular weights of all phthalocyanine complexes. Considering the mass spectra of all phthalocyanines, their molecular weights are M^{+} or $[M + H]^{+}$. Positive ion and linear mode MALDI-TOF mass spectra of compounds were obtained using 2,5-dihydroxy benzoic acid (DHB) or dithranol (DIT) as the MALDI matrix (Figures S5, S6, S10 and S11). The results of elemental analysis are consistent with the proposed structures of all phthalocyanine compounds. All characterization spectra are given in the supporting information (Figures S2-S11).

3.1. Spectrophoto- and fluorometric properties of phthalocyanines

Phthalocyanines can be characterized by UV–Vis spectroscopy because of their Q and B band absorptions in the UV–Visible region. The basic electronic absorption spectra of peripheral and non-peripheral tetra zinc phthalocyanine compounds were observed as a typical narrow Q band in the range of 650–700 nm. There were no wide specific changes in the Q band because the metal used in the phthalocyanine cores is Zn metal in all compounds.

Peripheral and non-peripheral tolyl coumarin zinc substituted phthalocyanine compounds showed good solubility in solvents such as ethyl acetate, pyridine, acetonitrile, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, and toluene. When the solvatochromic effects of phthalocyanines were examined, the most bathochromic effect was observed in pyridine compared to DMSO, while the hypsochromic effect was observed in dichloromethane (Fig. 1).

Due to the high absorption of the synthesized compounds in DMSO, the aggregation behavior of the studied phthalocyanines was investigated in DMSO at different concentrations. In non-

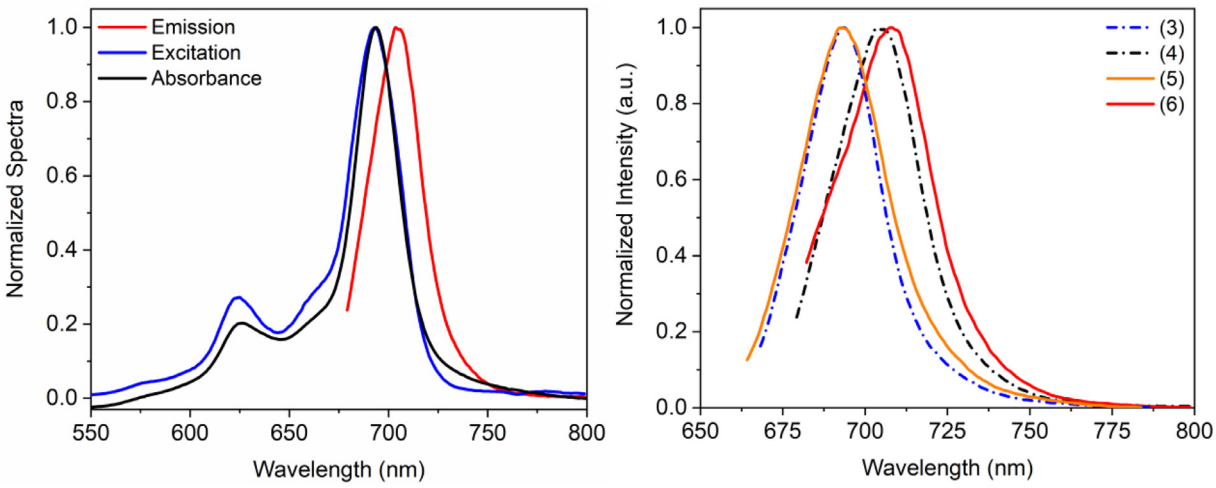


Fig. 2. Absorption, emission, and excitation spectrum of complex **4** (Left). Comparative emission spectra of synthesized compounds in DMSO (Right).

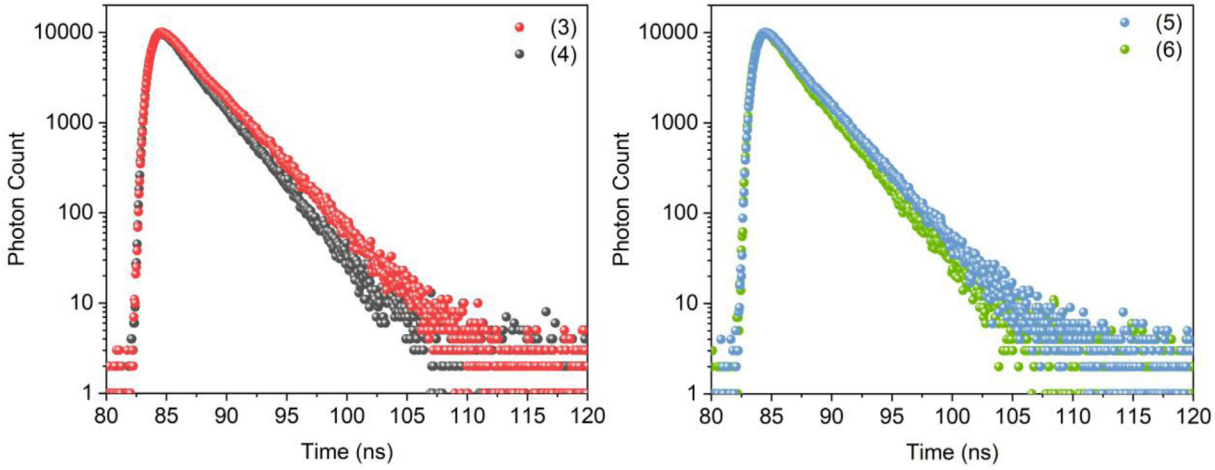


Fig. 3. Time correlated single photon counting (TCSPC) trace for coumarin phthalocyanines (**3**–**6**) in DMSO with residuals.

Table 1
Photophysical and photochemical parameters of phthalocyanines (**3**–**6**) in DMSO.

Sample	Φ_F	τ_F (ns)	k_F[a] (s^{-1}) × 10^8	Φ_d × 10^{-5}	Φ_Δ
(**3**)	0.33	2.89	0.11	14.93	0.51
(**4**)	0.18	2.49	0.07	2.51	0.62
(**5**)	0.25	2.68	0.02	3.83	0.40
(**6**)	0.11	2.42	0.05	1.75	0.52
Unsubs. ZnPc	0.20	1.22	0.16	2.61	0.67

[a] k_F is the transition rate constant for fluorescence. Values calculated using $k_{F=}\Phi_{F\,/}\,\tau_F$.

peripheral tolyl coumarin and tosyl coumarin substituted zinc phthalocyanines, the intensity of the Q band increased with increasing concentration, and no aggregation was observed. The intensity of the Q band increased with increasing concentration in peripheral tolyl coumarin substituted zinc phthalocyanine and no aggregation was observed. With the increase in the concentration of peripheral tosyl coumarin substituted zinc phthalocyanine, the intensity of the Q band increased, and aggregation was observed. Concentrations ranging from 1 × 10^{-5} to 1 × 10^{-6} M (in DMSO) for all phthalocyanine compounds comply with the Lambert-Beer law (Fig. 1).

3.2. Fluorescence spectra

Emissions of zinc phthalocyanine containing tolyl and tosyl coumarin in DMSO are similar compared to coumarin phthalocyanines in the literature [43–46]. Fluorescence emission peaks are 693 nm for (**3**) and 704 nm for (**4**). Compound **4** is 11 nm redshifted relative to (**3**). The peak for (**5**) is 694 nm while it is 708 nm for (**6**). Compound **6** is 14 nm redshifted to (**5**). Tosyl-coumarin bearing phthalocyanines (**5,6**) are more redshifted than tolyl-coumarin bearing phthalocyanines (**3,4**). Since the sulfonyl group has a high tendency to make H-bonds, the emission bands are more redshifted due to the H-bonding effect. The excitation spectra are the same and mirror image of the absorption spectra in DMSO for all phthalocyanines (Fig. 2).

Table 1

3.3. Fluorescence quantum yields and lifetimes

Fluorescent properties such as fluorescence quantum yield (Φ_F) and fluorescence lifetime (τ_F) are important parameters for photodynamic therapy applications because of the ability to visualize photosensitizers. The fluorescent quantum yield (Φ_F) was measured in DMSO for zinc(II) phthalocyanine compounds, and the results are given in Table 2. The fluorescence quantum yield of (**4**) in phthalocyanines containing tolyl-coumarin is lower than that

Table 2
Fluorescence quenching data for zinc phthalocyanine compounds (**3**–**6**, and unsubstituted **ZnPc**) in DMSO.

Sample	K_{sv}^{BQ} (M^{-1})	$K_q^{BQ}/10^{10}$ (M^{-1} s^{-1})	K_{sv}^{KI} (M^{-1})	$K_q^{KI}/10^{10}$ (M^{-1} s^{-1})
(3)	29.38	10.17	12.36	4.28
(4)	38.87	13.20	13.70	5.50
(5)	47.73	17.81	20.52	7.66
(6)	15.24	6.30	8.13	3.36
Unsubs. ZnPc	57.60	5.77	9.50	7.79

of (**3**). The fluorescence quantum yield of the compound **5** in tosyl-coumarin-containing phthalocyanines is higher than that of (**6**). When all phthalocyanine compounds were evaluated, only the compound **3** had a higher fluorescence quantum yield than the reference unsubstituted zinc phthalocyanine (**ZnPc**) compound.

Fluorescence lifetime (τ_F) refers to the average time a molecule stays in the excited state before emitting a photon. This parameter was measured for zinc phthalocyanines containing tolyl and tosylcoumarin using the time-dependent single photon counting method (TCSPC) in the DMSO solution. Time-dependent single-photon count (TCSPC) lifetime charts for synthesized phthalocyanines are shown in Fig. 3. The fluorescence of zinc(II) phthalocyanines led to a single exponential curve and the lifetime values of these phthalocyanines are given in Table 2. Both compounds **3** and **5** lifetime values are higher in nanoseconds (ns) than in the α forms. While the lifetime value of the unsubstituted reference zinc phthalocyanine (**ZnPc**) complex was 1.22 in DMSO [47], the lifetime values increased approximately twice with the addition of tolyl and tosyl-coumarin compounds to the structure. The fact that the compounds **4** and **6** had lower lifetime values than the compounds **3** and **5** can be interpreted as the result of the intermolecular interactions that occur when substituents are close to the phthalocyanine skeleton.

3.4. Singlet oxygen quantum yields

Singlet oxygen quantum yields (Φ_Δ) of tolyl and tosyl-coumarin substituted zinc(II) phthalocyanines were determined by a spectrophotometric method using 1,3-diphenylisobenzofuran (DPBF) as a quencher. There was no change in the Q band during the determination of singlet oxygen quantum yields, and the time-dependent decrease of DPBF absorbance at 417 nm confirmed that the complexes were not degraded during singlet oxygen studies (Fig. 4). When the singlet oxygen quantum yield values of all phthalocyanine compounds in the study were compared, the Φ_Δ value (Φ_Δ= 0.62) of the compound **4** was the highest compared to the singlet oxygen quantum yield values of its other derivatives, but the singlet oxygen quantum yields of all complexes were compared to the singlet oxygen quantum yields of the standard zinc phthalocyanine (**ZnPc**) compound. yield (0.67 in DMSO) [47] (Table 2).

Compounds **4** and **6** (α form) have higher singlet oxygen quantum yields than the compounds **3** and **5** (ß form). This is because the surface area of the phthalocyanine complex is narrowed by the binding of the substituents to the α position, and the Pc core can interact with DPBF in the solvent environment without steric hindrance. The reason why phthalocyanine complexes containing tolylcoumarin have higher singlet oxygen quantum yields than phthalocyanine complexes containing tosylcoumarin is the steric hindrance created by phthalocyanine groups interacting with each other as a result of intermolecular interactions of the tosyl group. For compounds **3** and **5**, the addition of the tosyl group to the C-3 position of the coumarin substituent changed the singlet oxygen production slightly and increased by one unit.

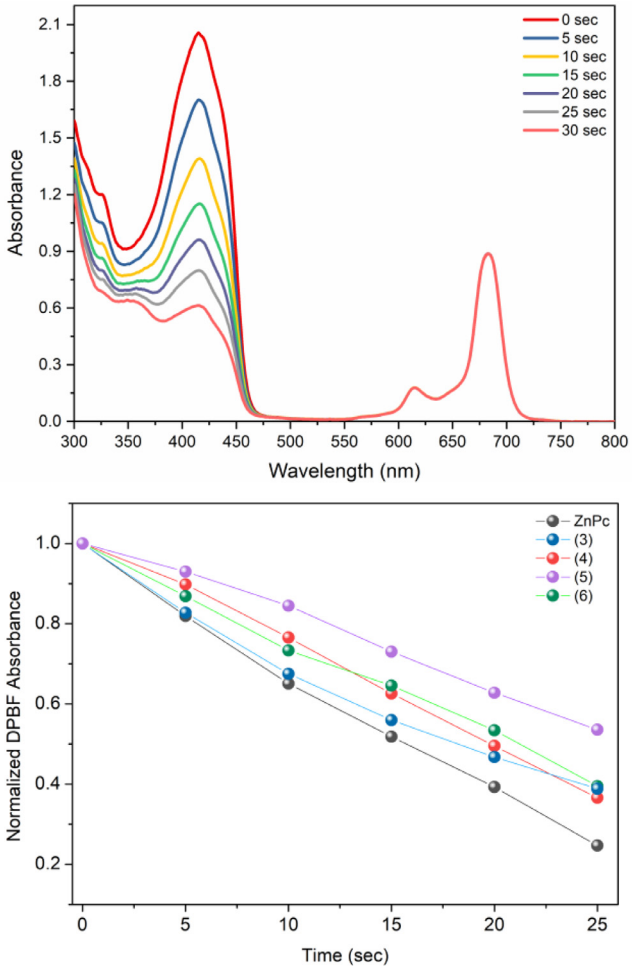


Fig. 4. Time-dependent (5 s) decreasing absorption (left) and slope graph (right) of DPBF compound in DMSO with compound **3** used to determine the singlet oxygen quantum yield. (concentration ~10 µM).

3.5. Photodegradation studies

The photodegradation quantum yield (Φ_d) is a measure of the stability of a molecule to light radiation. The degradation level of the molecules after irradiation is an important parameter for the target molecule to be used as a photosensitizer in photodynamic therapy applications. Phthalocyanine molecules produce singlet oxygen when exposed to irradiation with appropriate light, and the resulting singlet oxygen reduces phthalocyanine molecules through photooxidation reactions. The Q band intensity decreases linearly due to the degradation of phthalocyanines (Fig. 5). All photodegradation studies were carried out in DMSO.

The photodegradation quantum yield (Φ_d) values of all compounds are given in Table 2. Photodegradation quantum yields of peripheral and non-peripheral tolyl-/tosyl-coumarin phthalocya-

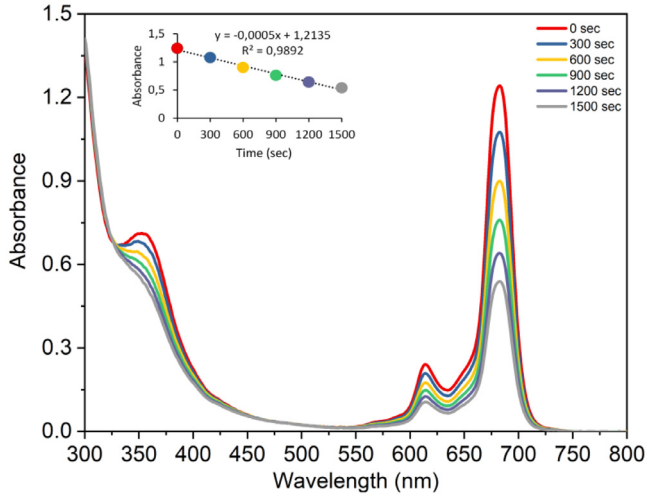


Fig. 5. Time-dependent photostability of the compound **3**. (Concentration ~10 μM).

nines are in the range of 10^{-4} to 10^{-5}, which is the ideal value range for photodynamic therapy applications. Tosyl-coumarin-containing phthalocyanines are more stable and light-fast than tolyl-coumarin-containing phthalocyanines. The tolyl group donates electrons to the ring and makes the phthalocyanine ring electron rich. The tosyl group on coumarin is strongly electron-withdrawing and causes electron deficiency in the phthalocyanine ring, which stabilizes the phthalocyanine structure against light. Non-peripheral coumarin substituted phthalocyanines (**4** and **6**) are more stable than their peripheral derivatives (**3** and **5**).

3.6. Structure-activity relationships in photophysicochemical parameters

The photophysical and photochemical parameters of 3-phenylcoumarin substituted zinc phthalocyanine complexes in the literature were investigated over the varying groups on the phenyl ring at the C-3 position of the coumarin core. Compound **3** fluorescence quantum yield is greater than the fluorescence quantum yield of the zinc metal coumarin-phthalocyanine compounds shown in Fig. 6, including the reference compound. With the addition of a sulfuryl group to the 3-phenylcoumarin derivative, singlet oxygen was also partially changed, and an increase was observed for singlet oxygen, while a decrease was observed for fluorescence quantum yield, lifetime, and photodegradation quantum yield.

Similar to the molecules in this study, Pişkin *et al*., the methoxy group from the para position to the phenyl ring at the C-3 position,

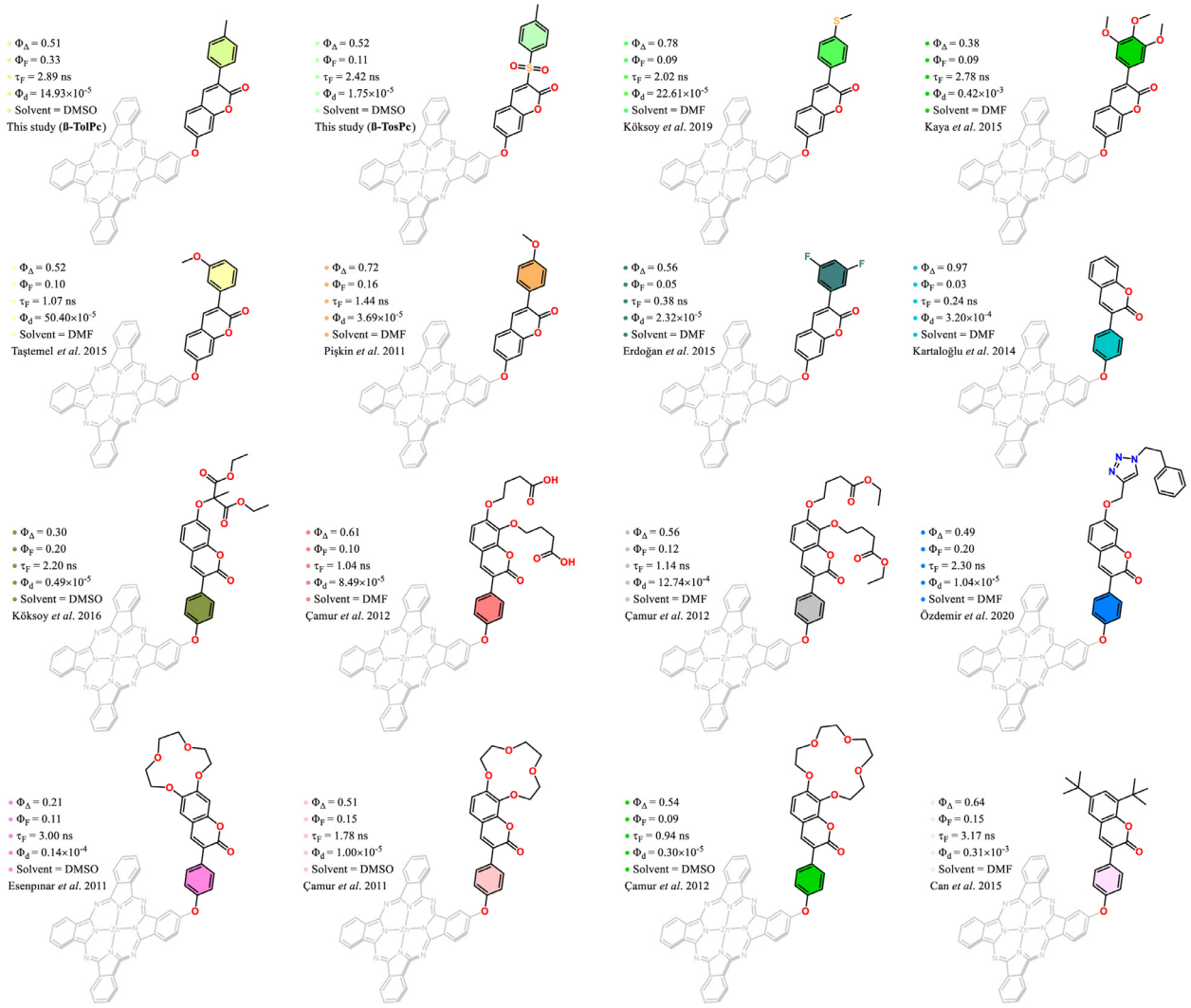


Fig. 6. Structure-activity relationships of peripheral 3-phenylcoumarin derivatives bearing zinc phthalocyanines in photophysicochemical parameters.

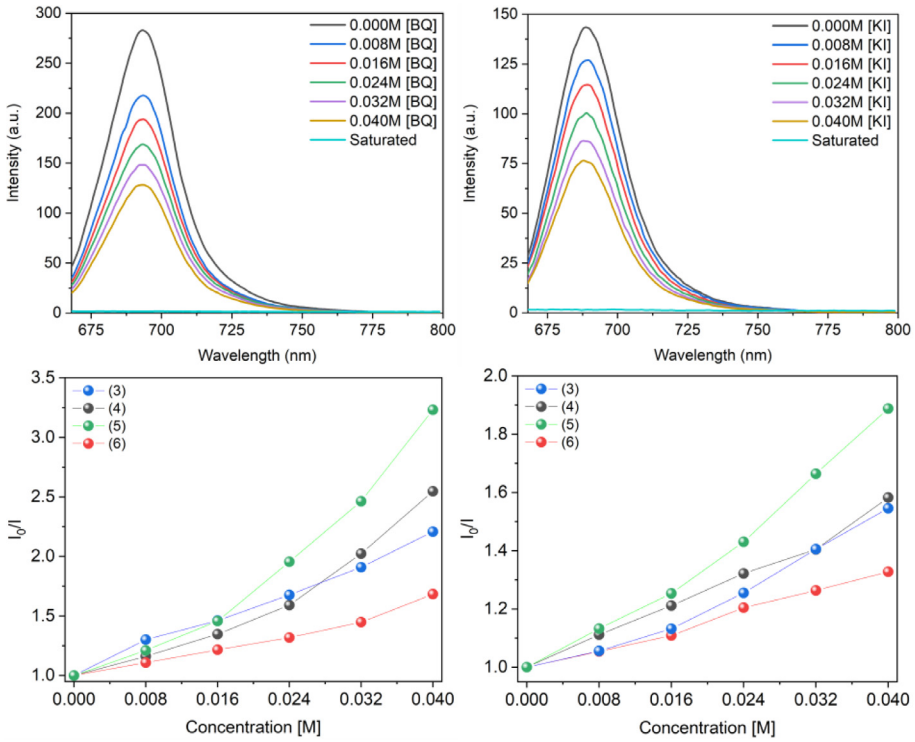


Fig. 7. (a) Fluorescence emission spectral changes of (**3**) by the addition of different concentration BQ in DMSO. (b) Fluorescence emission spectral changes of (**5**) by the addition of different concentrations KI in DMSO. (c) Stern-Volmer plots of phthalocyanines after quenching process.

and Köksoy et al. added a thiomethyl group [21,48]. Both added groups had positive effects on the singlet oxygen quantum yield. The thiomethyl functional group increased the fluorescence quantum yield and lifetime while decreasing the photostability, while the methoxy group increased the fluorescence quantum yield and photostability and decreased the lifetime value. Taştemel *et al*., like Pişkin's molecule, added a methoxy group from the meta position to the phenyl ring at the C-3 position and all photophysical and chemical parameters decreased [49].

According to Kaya *et al*., they added three methoxy groups from the meta position to the phenyl ring at the C-3 position, and all parameters except the photodegradation quantum yield decreased further compared to the methoxy–bearing derivatives only in the ortho or meta positions [50].

According to Kartaloglu *et al*., when they measured the values of the zinc phthalocyanine complex of the 3-(*p*-oxyphenyl)-coumarin compound, the singlet oxygen quantum yield was interestingly found to be 0.97 [51]. However, fluorescence quantum yield and lifetime values remained very low, since various enhancing functional groups were not found on coumarin. Similarly, Can *et al*. studied the phthalocyanine complex containing 3-(*p*-oxyphenyl)-coumarin, which has two *tert*–butyl groups on the coumarin core, and although the singlet oxygen quantum yield decreased, the fluorescence quantum yield and lifetime increased highly. Thanks to the *tert* groups, the molecules have also become more stable to light [45].

Koksoy *et al*. and Çamur *et al*. added ester derivatives to phenylcoumarin. When Çamur subsequently hydrolyzed the ester, the singlet oxygen quantum yield was higher than for the ester derivative. It is seen that the carboxyl group has the effect of increasing the singlet oxygen quantum yield compared to the ester groups, but the lifetime and fluorescence quantum yields of the esters decreased compared to their derivatives [52,53]. Erdogan *et al*. added two fluorine atoms from meta positions to the phenyl group and these electronegative atoms significantly reduced the fluorescence quantum yield and lifetime values [54]. On the other hand, Esenpınar *et al*. and Çamur *et al*. added 12-crown-4 from C6-C7 and C7-C8 carbons to 3-phenylcoumarins, respectively [55,56]. While the lifetime and photodegradation quantum yields of the crown ether functionalized coumarin-phthalocyanine complex synthesized by Esenpınar are higher, the singlet oxygen and fluorescence quantum yield of the phthalocyanine complex synthesized by Çamur are higher. Çamur *et al*. deepened their work and replaced 12-crown-4 with 15-crown-5 [53]. For the 15-crown-5 ether functionalized coumarin-phthalocyanine complex, the singlet oxygen quantum yield increased, while the fluorescence quantum yield, lifetime, and photodegradation quantum yield decreased. A correlation could not be established for the 12-crown-4 and 15-crown-5 ether-functionalized coumarin-phthalocyanine complexes.

In the light of all these results, the most efficient of the phthalocyanine complexes containing 3-phenylcoumarin are unsubstituted coumarin and coumarin phthalocyanine derivatives with functional groups such as methoxy, thiomethyl, and methyl attached to the phenyl ring in the C-3 position from the para position.

3.7. Fluorescence quenching studies

In fluorescence quenching studies, the energy of the lowest excited state of the benzoquinone compound as a quencher is greater than the ground state energy of the phthalocyanine compound, and energy transfer occurs from the phthalocyanine compound to the quencher in the environment. The phthalocyanine compound acts as an energy donor, while the benzoquinone or potassium iodide compounds are energy acceptors. With the energy transfer, there is a decrease in the fluorescence emission of the donor group. Since there are no emissions of benzoquinone or potassium iodide compounds, a new band does not occur.

Fluorescence quenching studies of zinc phthalocyanines containing tolyl and tosyl-coumarin were investigated using 1,4-

benzoquinone and potassium iodide as a quencher. The reduction of the emission spectrum due to quenching with BQ and KI is shown in Fig. 7 for compounds **3** and **5**.

The Stern–Volmer binding constant (K_{SV}) was highest for the unsubstituted reference **ZnPc** in both quenching measurements. This is probably because the energy of the system increases and the effect of energy transfer decreases with the addition of high-energy coumarin substituents to the structure. Compound **5** has the best binding constant after unsubstituted **ZnPc** in both benzoquinone [BQ] and potassium iodide [KI] measurements (Table 2).

Bimolecular quenching constants (k_q) are directly proportional to the Stern–Volmer binding constant and are in correlation. The emission bands of phthalocyanines decreased linearly with the addition of a quencher and exhibited ideal r coefficients. All these results suggest that phthalocyanines can bind to the proteins of cancer cells and interact with high-energy amino acids.

4. Conclusion

As a result, peripheral and non-peripheral zinc(II) phthalocyanine complexes were synthesized from 7–hydroxy-3-(*p*-tolyl)coumarin and 7–hydroxy-3-(*p*-tosyl)coumarin. positions. All synthesized compounds were characterized by elemental analysis, UV–vis, FT-IR, ^{1}HNMR , and MALDI-TOF. The aggregation behavior, fluorescence quantum yields and lifetimes, singlet oxygen quantum yields, photodegradation quantum yields, and fluorescent quenching properties of these new phthalocyanines were investigated in DMSO. All phthalocyanine compounds showed excellent solubility in common organic solvents such as chloroform, acetone, toluene, pyridine, dichloromethane, tetrahydrofuran, DMSO, and dimethylformamide. Photophysical and photochemical parameters of zinc(II) phthalocyanine compounds showed similar results to previously studied phthalocyanine derivatives. Singlet oxygen quantum yields of peripherally bound coumarin-substituted phthalocyanine complexes were higher than their non-peripheral derivatives. As a result of their photophysical and photochemical properties, coumarin-phthalocyanine complexes containing tolyl-/tosyl-groups can be used as photosensitizing candidates in photodynamic therapy and can be developed with targeted modifications.

Declaration of Competing Interest

There are no conflicts of interest to declare.

CRediT authorship contribution statement

Zehra Kazancıçok: Investigation, Data curation, Writing – original draft, Visualization. **Hatice Esra Güler:** Investigation, Writing – original draft. **Mücahit Özdemir:** Software, Investigation, Data curation, Writing – original draft, Visualization. **Mehmet Pişkin:** Methodology, Validation, Writing – original draft. **Mustafa Bulut:** Investigation, Writing – review & editing. **Bahattin Yalçın:** Conceptualization, Investigation, Resources, Writing – original draft. **Ümit Salan:** Conceptualization, Methodology, Validation, Writing – original draft, Supervision.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2022.134565.

References

[1] M. Lan, S. Zhao, W. Liu, C.S. Lee, W. Zhang, P. Wang, Photosensitizers for photodynamic therapy, Adv. Healthc. Mater. 8 (13) (2019) 1900132.
[2] H. Abrahamse, M.R. Hamblin, New photosensitizers for photodynamic therapy, Biochem. J. 473 (4) (2016) 347–364.
[3] S.-i. Ogura, K. Tabata, K. Fukushima, T. Kamachi, I. Okura, Development of phthalocyanines for photodynamic therapy, J. Porphyr. Phthalocyanines 10 (09) (2006) 1116–1124.
[4] C.M. Allen, W.M. Sharman, J.E. Van Lier, Current status of phthalocyanines in the photodynamic therapy of cancer, J. Porphyr. Phthalocyanines 5 (02) (2001) 161–169.
[5] R. Bonnett, Photosensitizers of the porphyrin and phthalocyanine series for photodynamic therapy, Chem. Soc. Rev. 24 (1) (1995) 19–33.
[6] E.A. Lukyanets, Phthalocyanines as photosensitizers in the photodynamic therapy of cancer, J. Porphyr. Phthalocyanines (2012).
[7] E. Güzel, Ü.M. Koçyiğit, B.S. Arslan, M. Ataş, P. Taslimi, F. Gökalp, M. Nebioğlu, İ. Şişman, İ. Gulçin, Aminopyrazole-substituted metallophthalocyanines: preparation, aggregation behavior, and investigation of metabolic enzymes inhibition properties, Arch. Pharm. (Weinheim) 352 (2) (2019) 1800292.
[8] A. Günsel, A.T. Bilgicli, B. Barut, P. Taslimi, A. Özel, İ. Gülçin, Z. Biyiklioglu, M.N. Yarasir, Synthesis of water soluble tetra-substituted phthalocyanines: investigation of DNA cleavage, cytotoxic effects and metabolic enzymes inhibition, J. Mol. Struct. 1214 (2020) 128210.
[9] A. Günsel, G.Y. Atmaca, P. Taslimi, A.T. Bilgicli, İ. Gülçin, A. Erdoğmuş, M.N. Yarasir, Synthesis, characterization, photo-physicochemical and biological properties of water-soluble tetra-substituted phthalocyanines: antidiabetic, anticancer and anticholinergic potentials, J. Photochem. Photobiol. A 396 (2020) 112511.
[10] A. Günsel, P. Taslimi, G.Y. Atmaca, A.T. Bilgicli, H. Pişkin, Y. Ceylan, A. Erdoğmuş, M.N. Yarasir, İ. Gülçin, Novel potential metabolic enzymes inhibitor, photosensitizer and antibacterial agents based on water-soluble phthalocyanine bearing imidazole derivative, J. Mol. Struct. 1237 (2021) 130402.
[11] E. Güzel, Ü.M. Koçyiğit, P. Taslimi, İ. Gülçin, S. Erkan, M. Nebioğlu, B.S. Arslan, İ. Şişman, Phthalocyanine complexes with (4-isopropylbenzyl) oxy substituents: preparation and evaluation of anti-carbonic anhydrase, anticholinesterase enzymes and molecular docking studies, J. Biomol. Struct. Dyn. 40 (2) (2022) 733–741.
[12] P.-C. Lo, M.S. Rodríguez-Morgade, R.K. Pandey, D.K. Ng, T. Torres, F. Dumoulin, The unique features and promises of phthalocyanines as advanced photosensitisers for photodynamic therapy of cancer, Chem. Soc. Rev. 49 (4) (2020) 1041–1056.
[13] J.C. Swarts, M.J. Cook, E.N. Baker, Metal-containing proteins, macrocycles, and Coordination Complexes in Therapeutic Applications and Disease, Hindawi, 2008.
[14] M. Özdemir, B. Karapınar, B. Yalçın, Ü. Salan, M. Durmuş, M. Bulut, Synthesis and characterization of novel 7-oxy-3-ethyl-6-hexyl-4-methylcoumarin substituted metallo phthalocyanines and investigation of their photophysical and photochemical properties, Dalton Trans. 48 (34) (2019) 13046–13056.
[15] N.L. Oleinick, A.R. Antunez, M.E. Clay, B.D. Rihter, M.E. Kenney, New phthalocyanine photosensitizers for photodynamic therapy, Photochem. Photobiol. 57 (2) (1993) 242–247.
[16] M. Çamur, M. Durmuş, M. Bulut, Highly singlet oxygen generative water-soluble coumarin substituted zinc (II) phthalocyanine photosensitizers for photodynamic therapy, Polyhedron 41 (1) (2012) 92–103.
[17] J. Zhang, C. Jiang, J.P.F. Longo, R.B. Azevedo, H. Zhang, L.A. Muehlmann, An updated overview on the development of new photosensitizers for anticancer photodynamic therapy, Acta Pharmaceutica Sinica B 8 (2) (2018) 137–146.
[18] M. Özdemir, G.Ö. Artuç, B. Akkurt, B. Yalçın, Ü. Salan, M. Durmuş, M. Bulut, Synthesis, characterization, photophysics, and photochemistry of peripherally substituted tetrakis (quinolinylethylenephenoxy)-substituted zinc (ii) phthalocyanines, New J. Chem. 45 (22) (2021) 9912–9921.
[19] P. Khoza, E. Antunes, T. Nyokong, Synthesis and photophysicochemical properties of zinc phthalocyanine derivatized with benzothiazole or carbazole photosensitizers, Polyhedron 61 (2013) 119–125.
[20] A. Grofcsik, P. Baranyai, I. Bitter, V. Csokai, M. Kubinyi, K. Szegletes, J. Tatai, T. Vidóczy, Triple state properties of tetrasubstituted zinc phthalocyanine derivatives, J. Mol. Struct. 704 (1–3) (2004) 11–15.
[21] M. Pişkin, M. Durmuş, M. Bulut, Highly soluble 7-oxy-3-(4-methoxyphenyl) coumarin bearing zinc phthalocyanines: synthesis and investigation of photophysical and photochemical properties, J. Photochem. Photobiol. A 223 (1) (2011) 37–49.
[22] S. Makhseed, A. Tuhl, J. Samuel, P. Zimcik, N. Al-Awadi, V. Novakova, New highly soluble phenoxy-substituted phthalocyanine and azaphthalocyanine derivatives: synthesis, photochemical and photophysical studies and atypical aggregation behavior, Dyes Pigm. 95 (2) (2012) 351–357.
[23] R. Murray, Coumarins, Nat. Prod. Rep. 6 (6) (1989) 591–624.
[24] J. Hoult, M. Payá, Pharmacological and biochemical actions of simple coumarins: natural products with therapeutic potential, General Pharmacol. 27 (4) (1996) 713–722.
[25] R.D. Murray, The naturally occurring coumarins, Fortschritte der Chemie organischer Naturstoffe Progress in the Chemistry of Organic Natural Products (2002) 1–619.
[26] O. Kayser, H. Kolodziej, Antibacterial activity of simple coumarins: structural requirements for biological activity, Zeitschrift für Naturforschung C 54 (3–4) (1999) 169–174.

[27] S.M. de Souza, F. Delle Monache, A. Smânia, Antibacterial activity of coumarins, Zeitschrift für Naturforschung C 60 (9–10) (2005) 693–700.
[28] C. Montagner, S.M. de Souza, C. Groposo, F. Delle Monache, E.F. Smânia, A. Smânia Jr, Antifungal activity of coumarins, Zeitschrift für Naturforschung C 63 (1–2) (2008) 21–28.
[29] S. Sardari, Y. Mori, K. Horita, R.G. Micetich, S. Nishibe, M. Daneshtalab, Synthesis and antifungal activity of coumarins and angular furanocoumarins, Bioorg. Med. Chem. 7 (9) (1999) 1933–1940.
[30] M.Z. Hassan, H. Osman, M.A. Ali, M.J. Ahsan, Therapeutic potential of coumarins as antiviral agents, Eur. J. Med. Chem. 123 (2016) 236–255.
[31] M. Özdemir, B. Köksoy, D. Ceyhan, K. Sayın, E. Erçağ, M. Bulut, B. Yalçın, Design and in silico study of the novel coumarin derivatives against SARS-CoV-2 main enzymes, J. Biomol. Struct. Dyn. (2020) 1–16.
[32] G. Borges Bubols, D. da Rocha Vianna, A. Medina-Remon, G. von Poser, R. Maria Lamuela-Raventos, V. Lucia Eifler-Lima, S. Cristina Garcia, The antioxidant activity of coumarins and flavonoids, Mini Rev. Med. Chem. 13 (3) (2013) 318–334.
[33] I. Kostova, S. Bhatia, P. Grigorov, S. Balkansky, V.S. Parmar, A.K. Prasad, L. Saso, Coumarins as antioxidants, Curr. Med. Chem. 18 (25) (2011) 3929–3951.
[34] I. Kostova, Synthetic and natural coumarins as antioxidants, Mini Rev. Med. Chem. 6 (4) (2006) 365–374.
[35] N. Sepehri, M. Mohammadi-Khanaposhtani, N. Asemanipoor, S. Hosseini, M. Biglar, B. Larijani, M. Mahdavi, H. Hamedifar, P. Taslimi, N. Sadeghian, Synthesis, characterization, molecular docking, and biological activities of coumarin–1, 2, 3-triazole-acetamide hybrid derivatives, Arch. Pharm. 353 (10) (2020) 2000109.
[36] A. Thakur, R. Singla, V. Jaitak, Coumarins as anticancer agents: a review on synthetic strategies, mechanism of action and SAR studies, Eur. J. Med. Chem. 101 (2015) 476–495.
[37] J.C. Menezes, M. Diederich, Translational role of natural coumarins and their derivatives as anticancer agents, Future Med. Chem. 11 (09) (2019) 1057–1082.
[38] J.G. Young, W. Onyebuagu, Synthesis and characterization of di-disubstituted phthalocyanines, J. Org. Chem. 55 (7) (1990) 2155–2159.
[39] R.D. George, A.W. Snow, Synthesis of 3-nitrophthalonitrile and tetra-α-substituted phthalocyanines, J. Heterocycl. Chem. 32 (2) (1995) 495–498.
[40] M. Özdemir, B. Köksoy, B. Yalçın, T. Taşkın, N.A. Selçuki, Ü. Salan, M. Durmuş, M. Bulut, Novel lutetium (III) phthalocyanine-coumarin dyads; synthesis, characterization, photochemical, theoretical and antioxidant properties, Inorganica Chim. Acta 517 (2021) 120145.
[41] M.S. Ağırtaş, Highly soluble phthalocyanines with hexadeca tert-butyl substituents, Dyes Pigm. 79 (3) (2008) 247–251.
[42] S. Wei, D. Huang, L. Li, Q. Meng, Synthesis and properties of some novel soluble metallophthalocyanines containing the 3-triflurometh ylphenyoxy moiety, Dyes Pigm. 56 (1) (2003) 1–6.
[43] M. Çamur, M. Bulut, M. Kandaz, O. Güney, Synthesis, characterization and fluorescence behavior of new fluorescent probe phthalocyanines bearing coumarin substituents, Polyhedron 28 (2) (2009) 233–238.
[44] M. Camur, M. Bulut, M. Kandaz, O. Güney, Effects of coumarin substituents on the photophysical properties of newly synthesised phthalocyanine derivatives, Supramol. Chem. 21 (7) (2009) 624–631.
[45] O.S. Can, E.N. Kaya, M. Durmuş, M. Bulut, High photosensitized singlet oxygen generating zinc (II) and indium (III) acetate phthalocyanines containing 6, 8-di-tert-butyl-3-(p-oxyphenyl) coumarin groups, J. Photochem. Photobiol. A 317 (2016) 56–67.
[46] M. Özdemir, A. Abliatipova, S. Benian, B. Yalçın, Ü. Salan, M. Durmuş, M. Bulut, 1, 2, 3-Triazole incorporated coumarin carrying metal-free, Zn (II), Mg (II) phthalocyanines: synthesis, characterization, theoretical studies, photophysical and photochemical properties, J. Photochem. Photobiol. A 403 (2020) 112845.
[47] I. Gürol, M. Durmuş, V. Ahsen, T. Nyokong, Synthesis, photophysical and photochemical properties of substituted zinc phthalocyanines, Dalton Trans. (34) (2007) 3782–3791.
[48] B. Köksoy, M. Durmuş, M. Bulut, Potential photosensitizer candidates for PDT including 7-oxy-3-thiomethylphenyl coumarino-phthalocyanines, Inorganica Chim Acta 498 (2019) 119137.
[49] A. Taştemel, B.Y. Karaca, M. Durmuş, M. Bulut, Photophysical and photochemical properties of novel metallophthalocyanines bearing 7-oxy-3-(m-methoxyphenyl) coumarin groups, J. Lumin. 168 (2015) 163–171.
[50] E.N. Kaya, M. Durmuş, M. Bulut, Novel 7-oxy-3-(3′, 4′, 5′-trimethoxyphenyl) coumarin substituted zinc (II) phthalocyanines: synthesis, characterization, photophysical and photochemical properties, J. Porphyr. Phthalocyanines 19 (10) (2015) 1114–1122.
[51] N. Kartaloğlu, A.A. Esenpınar, M. Bulut, Synthesis, characterization, and photophysical and photochemical properties of 3-(4-phenyloxy) coumarin containing metallo-and metal-free phthalocyanines, Turk. J. Chem. 38 (6) (2014) 1102–1117.
[52] M.A. Köksoy, B. Köksoy, M. Durmuş, M. Bulut, Preparation, characterization and photophysicochemical properties of novel tetra 7-(diethyl 2-methylmalonatoxy)-3-(p-oxyphenyl) coumarin-substituted zinc (II) and indium (III) chloride phthalocyanines, J. Organomet. Chem. 822 (2016) 125–134.
[53] M. Çamur, M. Durmuş, A.R. Özkaya, M. Bulut, Synthesis, photophysical, photochemical and electrochemical properties of crown ether bearing coumarin substituted phthalocyanines, Inorganica Chim. Acta 383 (2012) 287–299.
[54] T. Erdoğan, M. Bulut, M. Çamur, Novel phthalocyanines bearing 7-oxy-3-(3, 5-difluorophenyl) coumarin moieties: synthesis, characterization, photophysical and photochemical properties, J. Photochem. Photobiol. A 300 (2015) 6–14.
[55] A.A. Esenpınar, M. Durmuş, M. Bulut, Chromenone 12-crown-4 substituted zinc phthalocyanine complexes: investigation of spectral, photophysical and photochemical properties, Spectrochim. Acta Part A 81 (1) (2011) 690–697.
[56] M. Çamur, M. Durmuş, M. Bulut, Coumarino-12-crown-4 bearing phthalocyanine photosensitizers for singlet oxygen production, J. Photochem. Photobiol. A 222 (1) (2011) 266–275.