Synthesis, DFT Calculations, Photophysical, Photochemical Properties of Peripherally Metallophthalocyanines Bearing (2-(Benzo[d] [1,3] Dioxol-5-Ylmethoxy) Phenoxy) Substituents

Derya Gungordu Solgun, Umit Yildiko, and Mehmet Salih Agirtas

ABSTRACT

4-(2-(benzo[d] [1,3] dioxol-5-ylmethoxy) phenoxy) phthalonitrile was first prepared as a starting material. Then, this new phthalonitrile derivative was reacted with Zn and Co salts to obtain new phthalocyanine complexes. Phthalocyanine complexes were evaluated by fluorescence emission, extinction, and absorption measurements. Aggregation studies show compliance with the lambert-beer law in the concentration range studied for peripheral phthalocyanine compounds. The density functional theory calculations of the metallophthalocyanines compounds were performed using the B3LYP method- LanL2DZ basis set to derive structural optimization, HOMO-LUMO energy parameters, and nonlinear Optical properties. The calculated values of metallophthalocyanines with different center atoms were obtained close to each other. Molecular electronic surface maps of the studied compounds are mapped and discussed. The HOMO-LUMO energy gaps of our compounds studied are around 2.1 eV. The docking studies were performed with the phthalonitrile.

Introduction

Phthalocyanines have been a subject of interest for research for nearly a century. Promising results have been achieved in many areas. It is produced and used for fifty tons of paint industry worldwide. Besides, it is used in many fields such as catalyst, sensor, liquid crystal, optical data storage, solar cells. Photodynamic therapy, which is one of the cancer treatment methods, is being researched as the subject of intensive research. As an alternative to chemotherapy and radio therapy, which are currently used in cancer, photodynamic therapy is preferred in terms of nontoxic and daylight application. The synthesis of phthalocyanine compounds capable of producing appropriate singlet oxygen excites researchers. For this purpose, many scientific articles on phthalocyanines are published annually. Obtaining new functional and soluble phthalocyanines from these publications is seen as an important objective. Phthalocyanines are used to produce new and functional materials to meet today’s needs. New substitute groups are formed by connecting to the peripheral and non-peripheral or axial positions of the phthalocyanines. One of the main goals of phthalocyanine chemistry is to provide the use of this compound in photodynamic therapy for sensor and therapeutic purposes. In addition to the research of the present compounds, there is a need for alternative studies with the synthesis of new phthalocyanine...
compounds. DFT calculations of the synthesized compounds provide important information about the electronic structures of the compounds. In addition, it has an important role in revealing the non-linear optical properties of the compounds.

In this study, 4-(2-(benzo[d][1,3]dioxol-5-ylmethoxy)phenoxy)phthalonitrile compound was prepared as a starting material. Phthalocyanine complexes were synthesized from the reaction of this compound with zinc and cobalt salts under suitable conditions. The characterization of the obtained compounds, as well as aggregation, solubility, electronic absorption, fluorescence spectra, and computational properties, have been investigated. The synthesized phthalonitrile molecule also complied with the drug similarity rules and displayed acceptable predicted Absorption, Distribution, Metabolism, Extraction (ADME) properties.

**Experimental**

**General**

An electrothermal device was used to determine the melting point. Electronic transitions for the complexes were measured with a Hitachi U-2900 Spectrophotometer. FT-IR vibrations were determined by Thermo Scientific FT-IR spectrophotometer. The masses of the compounds were determined by the LC-MS TOF electrospray ionization technique. $^1$H and $^{13}$C NMR spectra were measured with an Agilent 400 MHz spectrometer. Fluorescence emission measurements were made in a Shimadzu RF-6000 spectrofluorophotometer. Chemicals and solvents were used commercially without purification.

**4-(2-(Benzo[d][1,3]dioxol-5-ylmethoxy)phenoxy)phthalonitrile (4)**

2-nitrophenol 1 (0.402 g, 2.89 mmol) and 4-nitrophthalonitrile 2 (0.500 g, 2.89 mmol) in 25 mL dimethylformamide (DMF) was stirred at room temperature under nitrogen atmosphere. After stirring for 30 min, piperonyl alcohol 3 (0.439 g, 2.89 mmol) was added into the mixture. After stirring for 15 min, K$_2$CO$_3$ (2.2 g, 16 mmol) was added into the mixture over a period of 2 h. The reaction mixture was further stirred for 42 h at room temperature. The reaction mixture was poured into cold water (150 mL) and stirred. The precipitate was filtered off, washed with water to neutralize it, the product was dried in a vacuum oven at 80°C. Melting point (MP): 153-156°C. Yield: 0.74 gr. The product is soluble in CHCl$_3$, CH$_2$Cl$_2$, acetonitrile, ethyl acetate, THF, DMF, DMSO. IR spectrum (cm$^{-1}$): 3086, 2926, 2868, 1643, 1598, 1487, 1234, 1159, 1116, 1085, 1035, 983. $^1$H NMR (400 MHz, DMSO-d$_6$): ($\delta$ : ppm) 8.18, 8.09, 8.06, 8.03, 7.81, 7.53, 7.01, 6.93, 6.01, 5.14, 3.30, 2.49. $^{13}$C NMR (400 MHz, DMSO-d$_6$): ($\delta$ : ppm) 162.09, 147.90, 147.82, 136.77, 136.47, 136.21, 129.51, 122.69, 120.94, 116.68, 116.63, 116.15, 109.27, 106.50, 101.59, 70.92, 40.63, 40.42, 40.22, 40.01, 39.80, 39.59, 39.38. HRMS (ESI); (M + H) calc. for C$_{22}$H$_{14}$N$_2$O$_4$: 370.36; found: 393.08 [M + Na]$^+$.  

**2, 10, 16, 24 – Tetrakis (2-(benzo[d][1,3]dioxol-5-ylmethoxy)phenoxy)phthalocyaninato) zinc (II) (5)**

A mixture of 4-(2-(benzo[d][1,3]dioxol-5-ylmethoxy)phenoxy)phthalonitrile 4 (0.050 g, 0.135 mmol) and ZnCl$_2$ (0.015 g) mixture was powdered in a quartz crucible and heated in a sealed glass tube for 5 min 210°C in the presence of DBU (2 drops). After reaching room temperature, the product was washed with hot and cold water, ethanol, methanol. The product soluble in THF was collected and the solvent was removed to obtain a green solid. This compound is soluble in dichloromethane, CHCl$_3$, THF, DMF, DMSO. MP >300°C. Yield: 0.020 g (38.46%). IR spectrum (cm$^{-1}$): 3084, 2929, 2868, 1643, 1598, 1487, 1234, 1159, 1116, 1085, 1035, 983. $^1$H
NMR (400 MHz, DMSO-d$_6$): ($\delta$: ppm) 7.24, 7.06, 6.85, 6.07, 6.00, 5.54, 3.32, 2.48, 1.34. UV-Vis (THF) $\lambda_{max}$ (log $\varepsilon$): 676 (5.08), 610 (4.44), 348 (4.85). HRMS (ESI); (M + H) calcd. for C$_{88}$H$_{56}$N$_8$O$_{16}$Zn: 1544.31; found: 1545.31 [M + H]$^+$. 

2, 10, 16, 24 – Tetrakis (2-([benzo[d] [1,3] dioxol-5-ylmethoxy] phenoxy) phthalocyaninato) cobalt(II) (6)

A mixture of 4-(2-([benzo[d] [1,3] dioxol-5-ylmethoxy] phenoxy) phthalonitrile 3 (0.050 g, 0.135 mmol) and CoCl$_2$ (0.015 g) mixture was powdered in a quartz crucible and heated in a sealed glass tube for 5 min 210$^\circ$/C. After reaching room temperature, the product was washed with hot and cold water, ethanol, methanol. The product soluble in THF was collected and the solvent was removed to obtain a green solid. This compound is soluble in ethanol, THF, DMF, DMSO. MP $>$ 300$^\circ$/C. Yield: 0.035 g (67.37%). IR spectrum (cm$^{-1}$): 3018, 2970, 1598, 1483, 1238, 1089, 1035, 920, 837, 734. UV-Vis (THF) $\lambda_{max}$ (log $\varepsilon$): 668 (5.20). HRMS (ESI); (M + H) calcd. for C$_{88}$H$_{56}$N$_8$O$_{16}$Co: 1539.31; found: 1540.41 [M + H]$^+$.

Results and discussion

Synthesis

Formulations of synthesized phthalocyanines and starting material are shown in Figure 1. 2-Nitrophenol, 4-nitrophenol, and piperonyl alcohol as the stoichiometric was reacted under nitrogen in the dimethylformamide to form 4-(2-([benzo[d] [1,3] dioxol-5-ylmethoxy] phenoxy) phthalonitrile. Zinc and cobalt phthalocyanines were then synthesized from this starting material. The reaction of zinc chloride and cobalt chloride salts with 4-(2-([benzo[d] [1,3] dioxol-5-ylmethoxy] phenoxy) phthalonitrile at 210$^\circ$/C yielded zinc and cobalt phthalocyanines. Vibration of aromatic (C–H) peak in the IR spectrum of compound number 4 is 3086 cm$^{-1}$, (CH$_2$) vibration 2926 cm$^{-1}$, (C= N) vibration 2233 cm$^{-1}$, (Ar– O– Ar) vibration 1249 cm$^{-1}$, (C= C) vibration peaks were observed at 1564 and 1500 cm$^{-1}$. The vibration peaks observed here are compatible with the expected structure. The most prominent change is observed in nitrile peaks after the conversion of this compound to zinc and cobalt phthalocyanine compounds. In the formation of phthalocyanine compounds that do not contain substituted nitrile groups, the nitrile peak present in the starting material completely disappears after the starting material is converted to phthalocyanine.$^{19}$ The nitrile peak observed in this study is also not seen in phthalocyanine compounds. In the formation of phthalocyanine compounds that do not contain substituted nitrile groups, the aromatic proton present in the starting material completely disappears after the starting material is converted to phthalocyanine.$^{19}$ The nitrile peak observed in this study is also not seen in phthalocyanine compounds. Vibration peaks for phthalocyanine 5 were observed as aromatic (C–H) at 3084 cm$^{-1}$, (CH$_2$) at 2926 cm$^{-1}$, (C= C) at 1598 cm$^{-1}$, and (Ar– O– Ar) at 1234 cm$^{-1}$. Finally, the vibrations of phthalocyanine 6 were observed at aromatic (C–H) peak 3018 cm$^{-1}$, (CH$_2$) 2970 cm$^{-1}$, (C= C) 1598 cm$^{-1}$, (Ar– O– Ar) peak at 1238 cm$^{-1}$ peaks appear to be in good harmony. 

As expected in the $^1$H NMR spectrum of compound 4 in DMSO-d$_6$, aromatic protons were observed as multiplets in the 8.18-6.93 ppm range. (CH$_2$) protons located between oxygen and oxygen among the aliphatic protons were observed at 6.01 ppm, while the (CH$_2$) peak bound to single oxygen was observed at 5.14 ppm. The $^{13}$C NMR spectrum of the compound in DMSO-d$_6$ also gives the peaks of the expected aromatic and aliphatic carbon atoms of the compound. Here, the carbon peaks of (C= N) were observed at 116.68-116.15 ppm, the aromatic carbon peaks at 162.09-106.50 ppm, the carbon peak of the (CH$_2$) atom between oxygen and oxygen at 101.59 ppm, and the carbon peak of single oxygen-bonded (CH$_2$) at 70.92 ppm. These observed peaks are in good agreement with the structure of the compound. $^1$H NMR and $^{13}$C NMR spectra of this compound are given in Figures 2 and 3. For zinc phthalocyanine compound 5, $^1$H NMR
Figure 1. Synthesis of compounds 4-6.
protons in DMSO-d$_6$ are observed as multiplets between 7.24-6.07 ppm, while aliphatic (CH$_2$) protons are observed at 6.00 ppm and 5.54 ppm. Due to its paramagnetic nature, $^1$H NMR measurements of compound 6 were not made.
Mass spectra of compounds (4-6) confirmed the proposed structure with the molecular ion being identified at 393.08 [M + Na]⁺, 1545.31 [M + H]⁺, and 1540.31 [M + H]⁺, respectively.

Another spectral instrument related to the structure of phthalocyanines is UV-Visible spectroscopy. It gives the absorbance value for the Q and B bands that are characteristic for phthalocyanines. While the Q band of the phthalocyanine compound is observed as a single peak when metal is attached, it is observed as a cleavage in the Q band in metal-free phthalocyanine compounds. For the phthalocyanines 5 and 6, the Q band absorption values in the THF solvent were measured as 676 and 668 nm, respectively. The B band of compound 5 was found to be 348 nm. These values are consistent with the tetra peripheral substitute structure. The absorption values of these compounds measured at different concentrations in THF are given in Figures 4 and 5. In addition, the electronic absorption of phthalocyanine 5 and 6 complexes in different solvents such as CH₂Cl₂, CHCl₃, THF, DMF, and DMSO is shown in Figures S1 and S2. As can be seen from these diagrams, these phthalocyanine compounds exist as monomers in the measured concentration range. This shows that it may be useful for some areas that wish to be non-aggregated (such as photodynamic therapy).

One of the foremost applications of phthalocyanine compounds is their use as a sensor agent in photodynamic therapy. For this application, the compound should exhibit fluorescence. The data obtained from fluorescence absorption, excitation, and emission spectra reveal fluorescence properties. Fluorescence absorption, excitation, and emission spectra of the zinc phthalocyanine compound observed is shown in Figure 6. Stokes shifts are within the expected range for the phthalocyanine compound. The Stokes shift detected in tetrahydrofuran for this phthalocyanine is 10 nm. The fluorescence emission was measured at 694 nm, while the excitation value was 682. The quantum yield of this compound (ΦF) was calculated as 0.30. This value is higher than the unsubstituted zinc phthalocyanine value. These spectral values are consistent with the studies given in the literature. These data strengthen the possibility that the compound can be used as a sensor.
Figure 5. Aggregation of compound 6 in $6.49 \times 10^{-6}$, $5.19 \times 10^{-6}$, $4.15 \times 10^{-6}$, $3.32 \times 10^{-6}$, $2.66 \times 10^{-6}$, $2.03 \times 10^{-6}$, $1.4 \times 10^{-6}$ concentrations.

Figure 6. Emission, excitation, and absorption zinc phthalocyanine 5 in DMSO at $10^{-6}$ M.
In addition to the fluorescence properties and fluorescence quantum efficiencies of the photosensors considered for photodynamic therapy, they can show an effective photosensor effect with their ability to produce singlet oxygen. In this study, a chemical method was used for the singlet oxygen production test to determine the photosensory ability of the zinc phthalocyanine compound. The singlet oxygen quantum yield ($\Phi_A$) of phthalocyanines 5 was determined in DMSO by using 1,3-diphenylisobenzofuran (DPBF) as a singlet oxygen quencher. During the measurements, the Q bands of phthalocyanine compound 5 did not change, while a decrease in DPBF absorbance was observed due to the reaction of singlet oxygen with DPBF (at 417 nm) (Figure 7). The $\Phi_A$ value of compound 5 ($\Phi_A = 0.57$) was found to be lower than Std-ZnPc. Here, one of the factors that can affect singlet oxygen production is substituted (2- (benzo [d] [1,3] dioxol-5-ylmethoxy) phenoxy) groups. The other is the electronic structure of the selected metal atom.

**Quantum chemical calculation instructions**

DFT calculations\textsuperscript{27,28} used in phthalocyanine compounds were carried out using the method coded B3LYP/LanL2DZ basis set of this method in the Gaussian 09 program.\textsuperscript{29} Within the scope of this study, optimization of metallo phthalocyanines in the gas phase and ground state was performed. Molecular orbital energies were calculated especially in phthalocyanine minimum energy optimization. The log and chk extension files obtained from the program were visualized with the program named Gauss View 6 and numerical data were transferred to tables.

**Structure details and analysis**

The molecular structure optimized by the method of the phthalocyanines 5,6 compound is shown in Figure 8, together with the bond length values. The optimized structural parameters calculated with the DFT/B3LYP - LanL2DZ basis set are determined. Here the planar structure of the
nucleus of the phthalocyanine compound is obtained. The bond lengths and angles between the optimized molecular atoms were compared for MPcs given in Table 1. When comparing the two MPcs, the bond lengths of the M-N atoms in phthalocyanine nuclei were calculated as 2.02 Å in Zn-N24 and 1.95 Å in Co-N24 with B3LYP/LanL2DZ, respectively. In the phthalocyanines, bond lengths were shorter. The small differences between them are due to the sensitivity of the methods and the metal atoms’ radii. In the optimization, the phthalocyanine nucleus has a planar structure and the metal atom is positioned at an angle of about 90. Dihedral angles of

Figure 8. The optimized molecular structure by DFT/B3LYP methods with LanL2DZ basis set, (a) bond length of phthalocyanine 6, (b) Mulliken charge of phthalocyanine 5.
Table 1. Theoretically obtained bond lengths (Å) and bond angles (°) of the molecules with the DFT/B3LYP method—LanL2DZ basis set.

| Atom groups | Bond lengths | Atom groups | Bond lengths |
|-------------|--------------|-------------|--------------|
|             | Compound 5   | Compound 6  |              |
| 1           | C29-C30      | 1.40        | C29-C30      | 1.40 |
| 2           | C68-C69      | 1.41        | C68-C69      | 1.42 |
| 3           | C54-C55      | 1.42        | C33-C21-C22  | 1.39 |
| 4           | O77-C75      | 1.41        | C127-0132-C133 | 1.41 |
| 5           | O64-C65      | 1.47        | C146-0145-C136 | 1.46 |
| 6           | O131-C133    | 1.48        | C1-N5-C4     | 1.48 |
| 7           | N6-C23       | 1.34        | C8-N12-C11   | 1.33 |
| 8           | N13-C14      | 1.34        | C21-C23-N24-C20 | 1.33 |
| 9           | N5-C1        | 1.39        | C69-C71-H76  | 1.33 |
| 10          | C69-H72      | 1.08        | C29-C30-H45  | 1.08 |
| 11          | C57-H61      | 1.08        | N12-(Zn, Co)-N5 | 1.08 |
| 12          | C114-H117    | 1.08        | N18-(Zn, Co)-N12 | 1.08 |
| 13          | (Zn,Co)-N24  | 2.02        | N24-(Zn, Co)-N18 | 1.95 |

phthalocyanines 5 were calculated as \( N_{18}-Zn_{41}-N_{24}-C_{23} \) 178.4°, and \( N_{5}-Zn_{41}-N_{24}-C_{20} \) – 178.04°. Dihedral angles of Co-Pc were calculated as \( N_{5}-Co_{169}-N_{24}-C_{20} \) 0.98° and \( N_{18}-Co_{169}-N_{24}-C_{23} \) 179.73° with LanL2DZ basis set. Both MPs with the basis set demonstrate that the phthalocyanine compound is planar in accordance with the dihedral angles of about 180°.30

**HOMO and LUMO analysis**

Quantum chemical calculations are widely used to calculate basic electronic parameters related to orbitals in the molecule. As frontier orbital molecules, the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO) are important.31 However, by using these values, the activity parameters and energy deficit of the molecule are calculated and the chemical character of the molecule is determined. Perturbation MO theory is based on the energy difference between HOMO and LUMO.32–34 The closer the energy levels of the interacting molecular orbitals to each other, the stronger the interaction. That is, the smaller the HOMO - LUMO energy difference, the stronger the interaction of the reactants and the easier the reaction.35

The calculated results and their comparison for the MPcs are presented in Table 2. Figures 9 and 10 is the density orbital representation of the HOMO and LUMO of the compounds 5-6 in both methods. LUMO + 1 and HOMO-1 graphs of the compound were also taken. Frontiers orbitals of the compound 5, HOMO –4.96 eV LUMO –2.82 eV value and for compound 6, HOMO –4.96 eV LUMO –2.77 eV values at DFT/B3LYP/LanL2DZ level were calculated. The HOMO and LUMO, frontiers orbitals also help determine the degree of activity and interaction of the molecule with other species.36–38 HOMO, LUMO, and the chemical reactivity descriptors of the compounds 5-6 calculated in the DFT method were correlated and shown in Figure 11. In the comparison of band gap and other orbital energies, it was slightly higher in phthalocyanine with cobalt atoms.

**Nonlinear optics analysis**

The dipole moment, which is the specialty of energy, is applied intramolecular.39–41 The dipole moment consists of Van der Waals-type intermolecular interactions and intermolecular attraction is strong. The electronic dipole moment and total dipole moment are listed in Table 3.

The dipole moment, molecular polarization and hyperpolarization values should be calculated to determine nonlinear optical properties.33,42–44 In the compound 5, the parameters are
respectively $\mu = 8.4 \text{ D}$, $\alpha = 598.6 \text{ au}$, $\beta = 5.13 \times 10^{-31} \text{ esu}$. Also, in the compound 6 the parameters are respectively $\mu = 8.4 \text{ D}$, $\alpha = 593.5 \text{ au}$, $\beta = 5.08 \times 10^{-31} \text{ esu}$. Compound 5 was higher than compound 6 due to the difference in the central atom, dipole moment and other related parameters. According to these values, the molecule has parametric quantities that can be considered as non-linear optics materials.

### Molecular electrostatic potential

Molecular electrostatic potential (MEP) maps provide information about the electronic charge distribution of a molecule. The density of the electron distribution on the molecule is useful for illuminating bonds with descriptors such as polarity, electronegativity. The electronic structure and molecular reactivity of complex molecules can exhibit rich topographic properties.32,42,44–46

In this study, electrophilic potential (MEP) maps of three phthalocyanine molecules were obtained. As shown in Figure 7 they are visualized with MEP maps at the DFT/B3LYP method with LanL2DZ basis set using the GaussView 6.0 software. The MEP maps show that the region characterized by the blue color around the Zn and Co atoms has positive values. The red regions on the map indicate the region rich in electrons. The aromatic ring region shows an almost neutral potential, most of which is represented by a yellow-green color. Contour maps of phthalocyanines confirm negative and positive potential parameters in accordance with the electrostatic potential map (ESP). The phthalocyanine nucleus in the structures shows the delocalized structure and high stabilization with green-yellow colors in color. Moreover, in the MEP maps, the negative potentials are mainly found in, for example, O-107 and O-118, while the potential occurring around the H-147 atom is the most positive. In terms of electronegativity, oxygen atoms can be interpreted higher than other atoms.

### Molecular docking analysis

The protein crystal structure of different enzymes was selected for the compound 4 in the Protein Data Bank (http://www.rcsb.org). From these complexes, PDB codes were selected and retrieved from the Protein Data Bank. As protein receptors, human carbonic anhydrase isozyme II (PDB ID: 6R6F), acetylcholinesterase (PDB ID: 4RVK), and butyrylcholinesterase (PDB ID: 6SAM) enzymes were used. The Docking studies were performed using the commercial software Schrodinger suite Maestro version 10.2.47

Ligand preparation and protein preparation via LigPrep, and Protein preparation modules were used in accordance with the previous studies.48–50 In addition, enzyme inhibition in-silico study compound 4 was conducted in this study. Enzyme binding affinity was found as $-5.24$ and
7.67 kcal/mol and gave well results. The best docking poses were selected for analysis of interactions, and protein-ligand interaction was presented with Discovery Studio Client 2017 software.

Computational ADME modeling is a very mature but still-developing field. In silico ADME tools are routinely applied to drug design. The synthesized compound 4 also complied with the drug similarity rules and displayed acceptable predicted ADME properties. In the analysis made on SwissADME: Drug similarity was evaluated a free web tool to evaluate. In this analysis, it was found to be compatible compared to the Lipinski (Pfizer) filter. The online servers SwissADME
Figure 10. MEP reactive sites calculated at DFT/B3LYP methods with LanL2DZ basis sets (a) phthalocyanine 5 and (b) phthalocyanine 6.
were employed to check the chemo-informatics and biological properties of this ligand molecule. The results in Table 4 show that the compounds are compatible with MW 370.36 g/mol (<500), LogP values according to the Lipinski rule with 1.9 (<5), and HBA 6 (<10). Topological PSA 84.50 < 140 A^2, and ABS is 79.85%.

The compound 4 with (6SAM BChE) had the most effective coupling score (-7.69 kcal/mol) and good binding affinity was obtained (Figure 12). Here, when the ligand interactions with protein residues are evaluated, the strongest bindings were line up as TRP82 3.09 Å conventional...
Figure 12. The interaction 3D View mode between compound 4 and enzymes a) the aromatic surface on the receptor of hCA I b) the hydrogen bonds donor/acceptor surface on hCA I enzyme interactions c) the hydrogen bonds donor/acceptor surface on d) the AChE enzyme interactions the aromatic surface on the receptor.

Figure 13. 2D View of the interaction modes between compound 4 and enzymes, a) phthalonitrile -hCA II, b) phthalonitrile -AChE, c) phthalonitrile -BChE, d) types of interaction between molecular.
hydrogen bond, TRP430 3.05 Å conventional hydrogen bond, GLY116 4.03 Å Amide-pi Stacked. TRP82-4.30 Å residues and nitrile groups on the ligand were observed to frame the H-bond side chain.

In docking of the compound with another enzyme (6R6F AC II), the glide score was calculated to be $-6.219 \text{kcal/mol}$. TRP5 2.11 Å traditional hydrogen bond, HIS4 2.42 Å conventional hydrogen bond, GLN92 2.59 Å traditional hydrogen bond, HIS64 4.83 Å pi-pi T-shaped, HIS94 4.86 Å pi-pi T-shaped, ALA65 4.89 Å pi-alkyl, LEU198 4.91 Å pi-alkyl, VAL121 4.54 Å formed pi-alkyl bonds.

Finally, in another docking with receptor 4RVK AChE, a docking score of $-5.24 \text{kcal/mol}$ was obtained. This docking complex, respectively ASP148 exhibited interactions with 4.84 Å pi-anion, GLU91 4.47 Å pi-anion, VAL23 4.30 Å pi-alkyl, LEU137 5.26 Å and 5.37 Å pi-alkyl, LEU15 4.05 Å pi-alkyl, and TYR86 3.08 Å conventional hydrogen bonds (Figure 13). Here, it was determined that the phthalonitrile compound on the three enzyme proteins exhibited good performance in enzyme inhibition. The ligand-receptor binding score in the docking study also correlated well with the published data.53,54

**Conclusion**

In this study, 4-(2-(benzo[d][1,3]dioxol-5-ylmethoxy)phenoxy)phthalonitrile (4) was synthesized as a starting material. From the reaction of this starting material with zinc and cobalt salts, zinc(II) and cobalt(II) phthalocyanine complexes (5-6) were synthesized. Compounds (4-6) were characterized by IR, UV, NMR and mass spectroscopy methods. Non-agglomeration properties of phthalocyanine compounds and fluorescent emission properties of zinc phthalocyanine compounds and its ability to produce singlet oxygen were investigated. Quantum chemical calculations show that both phthalocyanine complexes have very similar structures in the gas phase. We used the DFT/B3LYP method with the LanL2DZ basis set to determine and analyze the geometric optimization of MPcs. The dipole moments of compounds 5–6 were calculated as 8.00 and 8.38 Debye, respectively. This value gives the potential to be used as nonlinear material. In addition, the starting material phthalonitrile molecule was also docking studied in terms of compliance with drug similarity rules and it was observed that it exhibited acceptable predicted ADME properties.

**ORCID**

Ümit Yıldırım  
http://orcid.org/0000-0001-8627-9038

Mehmet Salih Ağırtaş  
http://orcid.org/0000-0003-1296-2066

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