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DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF NOVEL WATER-SOLUBLE QUINOLINE-BASED CONJUGATES WITH ANTIOXIDANT, ANTIMICROBIAL, AND DNA-BINDING ACTIVITIES

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Considering the extremely valuable biological and pharmaceutical properties of quinolines, novel water-soluble quinoline-based conjugates were designed and synthesized. In vitro antioxidant activities, such as free radical scavenging, metal chelating, and reducing-power activities, of the newly synthesized compounds (**WQ-1**, **WQ-2**, **WQ-3**, **WQ-4**, and **WQ-5**) were determined. Although the highest scavenging activity (41.21 ± 1.18%) and chelating activity (23.53 ± 0.97%) at a concentration of 500.0 μg/ml were observed in **WQ-4**, it was determined that **WQ-5** had the highest reducing-power ability (0.417 ± 0.0116). The synthesized compounds were also tested for their antimicrobial activities against two Gram-positive and two Gram-negative bacteria, and it was determined that only **WQ-3** showed low activity against *Enterococcus hirae* and *Staphylococcus aureus*. DNA-binding activities of the compounds were also studied using calf thymus DNA (CT-DNA). Additionally, the three-dimensional geometries and some electronic properties of the synthesized compounds were investigated with the density functional theory approach at B3LYP/6-31++G(d,p) level of theory.

Keywords: quinoline-triazole; synthesis; antioxidant; antimicrobial; electronic properties

ДИЗАЈН, СИНТЕЗА И БИОЛОШКА ЕВАЛУАЦИЈА НА НОВИ ВОДОРАСТВОРЛИВИ КОНЈУГИРАНИ ПАРОВИ БАЗИРАНИ НА ХИНОЛИН СО АНТИОКСИДАТИВНА, АНТИМИКРОБНА И АКТИВНОСТ ЗА ВРЗУВАЊЕ СО DNA

Имајќи ги предвид исклучително вредните биолошки и фармацевтски својства на хинолините, беа дизајнирани и синтетизирани нови водорастворливи конјугирани парови базирани на хинолин. Во условите *in vitro* беа определени антиоксидациските активности на новосинтетизираните соединенија (**WQ-1**, **WQ-2**, **WQ-3**, **WQ-4** и **WQ-5**) како што се способноста за неутрализација на слободни радикали, комплексообразувачка активност и редукциска способност. Иако кај **WQ-4** беа забележани највисоки активности на неутрализација на радикали (41,21 ± 1,18%) и комплексообразувачка активност (23,53 ± 0,97%) при концентрација од 500,0 μg/ml, утврдено е дека **WQ-5** има најголема редукциска способност (0,417 ± 0,0116). Синтетизираните соединенија беа тестирани и за нивната антимикробна активност против две Грам-позитивни и две Грам-негативни бактерии, при што беше утврдено дека само **WQ-3** покажува ниска активност против *Enterococcus hirae* и *Staphylococcus aureus*. Активностите на врзување со DNA беа испитани користејќи DNA од теле (CT-DNA). Дополнително, тридимензионалната геометрија и некои електронски својства на синтетизираните соединенија беа проучени со примена на теоријата на функционал на густина на ниво B3LYP/6-31++G(d,p).

Клучни зборови: хинолин-триазол; синтеза; антиоксидациско средство; антимикробна активност; електронски својства

1. INTRODUCTION

As a naturally occurring skeleton, quinoline attracts many researchers' attention due to its use in pharmaceuticals, agrochemicals, functional materials, and ligands in transition-metal catalysts.[1-3] Molecules bearing quinoline skeletons have wide ranging pharmaceutical activities; for example, they have been reported to have antiviral,[4] antitubercular,[5] antimalarial,[6] anti-inflammatory,[7] antifungal,[8] anticancer,[9] antibiotic,[10] and antihypertensive[11] activities. Thus, the development of efficient methodologies for the preparation of substituted quinolines is very important in organic synthesis.

Triazoles tend to interact with enzymes, proteins, and receptors in organisms, and their derivatives possess a variety of biological activities, including anticancer,[12] antiviral,[13] antitubercular,[14] antibacterial,[15] and anti-inflammatory[16] activities. The 1,2,3-triazole moiety is of great importance in the fields of chemistry and chemical biology due to its unique properties, inert nature, and ability to mimic amide bonds.[17] Some important drugs that retain the 1,2,3-triazole moiety in their core structures, such as tazobactam (antibiotic) and rufinamide (anticonvulsant), are well known (Figure 1). The most efficient method for the synthesis of 1,2,3-triazoles is the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of organic azides with alkynes, which forms only the 1,4-disubstituted 1,2,3-triazoles selectively.[18]

The molecular hybridization strategy is widely used in drug design and development based on the connection of two or more pharmacophoric moieties of different bioactive substances in a single chemical entity. This strategy can produce new hybrid compounds with improved affinity and efficacy compared to the parent drugs and can help to reduce undesired side effects.

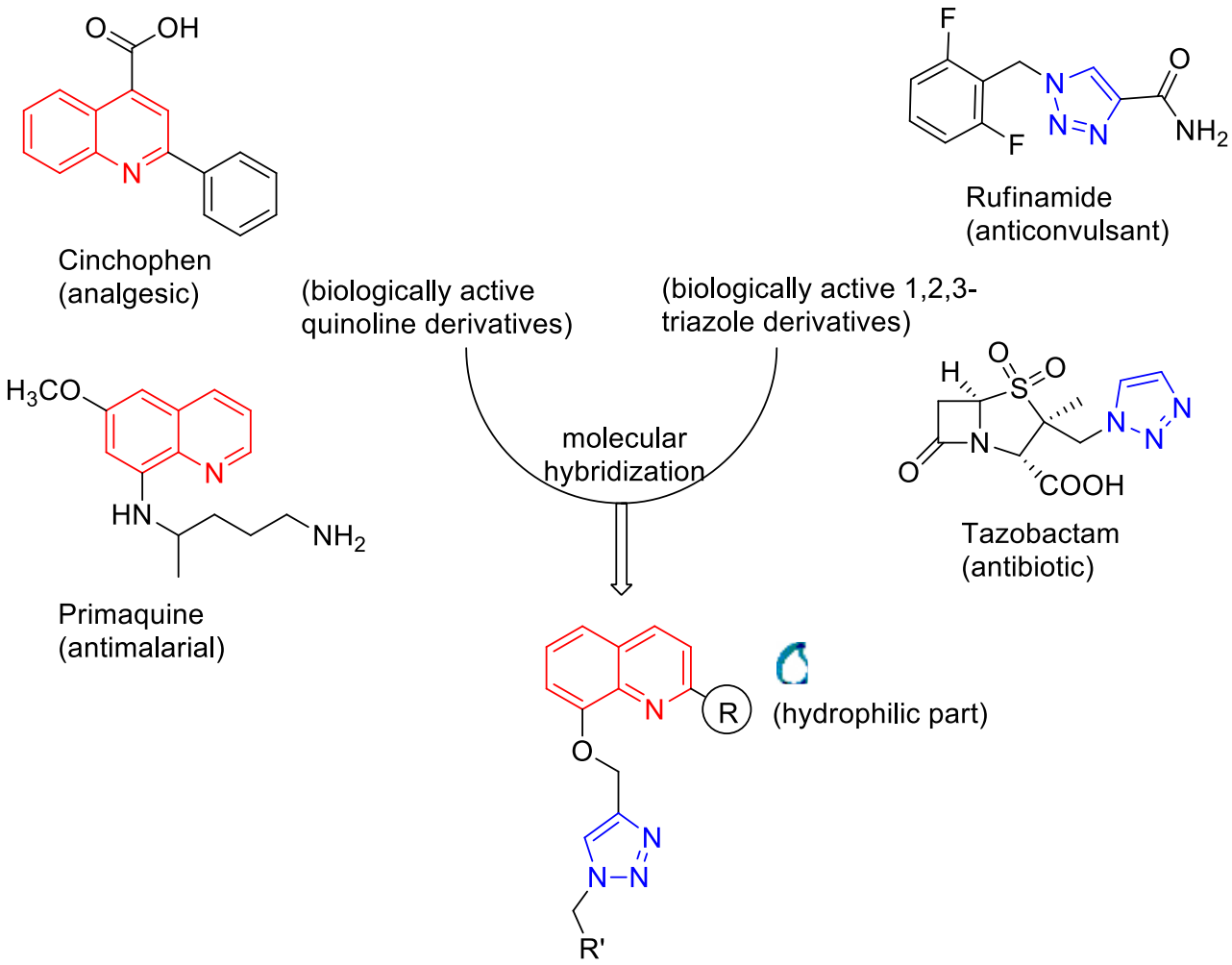


Fig. 1. Design of novel water-soluble quinoline-triazole hybrids

As part of our ongoing work to synthesize new chemical scaffolds of biological importance, we have designed hybrid structures of quinoline and triazoles. The quinoline skeleton was retained as a core pharmacophore across all derivatives. Designing water-soluble quinoline-based conjugates may enhance their biological potential while providing valuable insights into structure–activity relationships. Diglycol monomethyl ether moieties were introduced to enhance aqueous solubility, facilitating biological evaluation. Anthracene and pyrene units were attached to the target molecules via linker groups, including acetyl and the triazole ring, which are good centers for hydrogen-bonding interactions. Furthermore, triazoles are very stable to both metabolic and chemical degradation, being inert to hydrolytic, oxidizing, and reducing conditions.

In particular, investigating antioxidant and antimicrobial activities, along with DNA-binding properties, can provide comprehensive information on their therapeutic potential. Furthermore, computational studies, such as density functional theory (DFT), can help to understand the electronic properties and geometric structures of the synthesized compounds, supporting the interpretation of experimental findings.

In this study, novel water-soluble quinoline-based conjugates were designed, synthesized, and evaluated for their antioxidant, antimicrobial, and DNA-binding activities, and these efforts were complemented by theoretical studies to explore their structural and electronic characteristics.

2. EXPERIMENTAL

2.1. *Chemistry*

All chemicals and solvents were purchased from commercial suppliers and used without purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on an Agilent 400 MHz spectrometer. ^{1}H (400 MHz) and ^{13}C NMR were recorded in chloroform-d ($CDCl_3$), and the chemical shifts were reported in ppm relative to tetramethylsilane ($Si(CH_3)_4$) as the internal standard. LC/MS-MS spectra were recorded on a Thermo Scientific Q Exactive mass spectrometry. Melting points were recorded in open glass capillaries on a Stuart SMP3 instrument. Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 FT-IR spectrometer in ATR mode.

Flash column chromatography was performed using thick-walled glass columns and silica gel (60-mesh; Merck). The reactions were monitored by thin-layer chromatography (TLC) using Merck 0.2-mm silica gel 60 F254 analytical aluminum plates, and spots were visualized by UV light.

2.1.1. *Synthesis of* ***WQ-1***

2.1.1.1. *2-(2-(2-methoxyethoxy)ethoxy)-8-(prop-2-yn-1-yloxy)quinoline,* ***3***

8-(prop-2-yn-1-yloxy)quinolin-2-ol, **2** (199 mg, 1 mmol), which was synthesize according to method reported in the literature,[19] was dissolved in 10 ml CH_3CN. K_2CO_3 (207 mg, 1.5 mmol) was added and the mixture was refluxed for 30 min. Then, 2-(2-methoxyethoxy)ethyl 4-methylbenzenesulfonate (274 mg, 1 mmol) was added and the reaction was stirred at reflux overnight. The reaction was monitored by TLC. After the reaction mixture was cooled, it was filtered and the solvent was removed. The product **3** was purified by column chromatography using silica gel and EtOAc/hexane (1:3)

White solid; 68 % yield; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7,96 (d, J = 8.9 Hz, 1H, Ar–H), 7.39 (dd, J = 7.8 and J = 1.5 Hz, 1H, Ar–H), 7.29 (t, J = 7.8 Hz, 1H, Ar–H), 7.26–7.23 (m, 1H, Ar–H), 6.96 (d, J = 8.8 Hz, 1H, Ar–H), 5.01 (d, J = 2.4 Hz, 2H, CH_2O), 4.72–4.70 (m, 2H, CH_2O), 3.94–3.91 (m, 2H, CH_2O), 3.75–3.73 (m, 2H, CH_2O), 3.59–3.57 (m, 2H, CH_2O), 3.38 (s, 3H, OCH_3), 2.52 (t, J = 2.4 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.2, 151.9, 138.9, 138.4, 126.4, 123.7, 121.4, 114.2, 113.6, 79.0, 75.7, 71.9, 70.5, 69.7, 65.1, 59.1, 57.8. LC-MS/MS: Anal. Calcd. for $C_{17}H_{19}NO_4$ $[M+H]^+$: *m/z* 302.1387. Found: *m/z* 302.1392. IR υ_{max} (neat, cm^{-1}): 3273, 2924, 2873, 2118, 1606, 1504, 1431, 1354, 1242, 1089, 920, 752, 584.

2.1.1.2. *8-((1-(anthracen-9-ylmethyl)-1H-1,2,3-triazol-4-yl)methoxy)-2-(2-(2-methoxyethoxy) ethoxy)quinoline,* ***WQ-1***

2-(2-(2-methoxyethoxy)ethoxy)-8-(prop-2-yn-1-yloxy)quinoline (100 mg, 0.3 mmol) and 9-(azidomethyl)anthracene (70 mg, 0.3 mmol) were dissolved in 5 ml of THF:H_2O (4:1); $CuSO_4{\cdot}5H_2O$ (13 mg, 0.5 mmol) and sodium ascorbate (20 mg, 0.1 mmol) were added, and the reaction mixture was stirred at room temperature for 24 h. After the experiment was terminated, the solvent was evaporated. The product **WQ-1** was purified by column chromatography using EtOAc:hexane (1:1).

White solid; mp 124–126 °C; 81% yield; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.59 (s, 1H, Ar–H), 8.32–8.30 (m, 2H, Ar–H), 8.10–8.07 (m, 2H, Ar–H), 7.88 (d, J = 8.9 Hz, 1H, Ar–H), 7.62–7.58 (m, 2H, Ar–H), 7.55–7.51 (m, 2H, Ar–H), 7.29 (s, 1H,

Ar–H), 7.27 (dd, *J* = 8.0 and *J* = 1.3 Hz, 1H, Ar–H), 7.17 (t, *J* = 7.9 Hz, 1H, Ar–H), 7.08 (dd, *J* = 7.8 and *J* = 1.3 Hz, 1H, Ar–H), 6.87 (d, *J* = 8.8 Hz, 1H, Ar–H), 6.56 (s, 2H, CH_2N), 5.31 (s, 2H, CH_2O), 4.34–4.32 (m, 2H, CH_2O), 3.64–3.60 (m, 4H, CH_2O), 3.54–3.52 (m, 2H, CH_2O), 3.37 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.0, 152.5, 144.8, 138.8, 131.4, 130.8, 129.9, 129.5, 127.7, 126.2, 125.4, 123.8, 123.7, 123.0, 122.2, 120.8, 113.5, 113.3, 113.2, 71.9, 70.3, 69,6, 64.6, 64.2, 59.0, 46.5. LC-MS/MS: Anal. Calcd. for $C_{40}H_{36}N_4O_4$ $[M+H]^+$: *m/z* 637.2817. Found: *m/z* 637.2809. IR υ_{max} (neat, cm^{-1}): 3050, 2877, 1618, 1576, 1509, 1430, 1339, 1198, 1051, 826, 727.

2.1.2. *Synthesis of* ***WQ-2***

2-(2-(2-methoxyethoxy)ethoxy)-8-(prop-2-yn-1-yloxy)quinoline **3** (100 mg, 0.3 mmol) and 1-(azidomethyl)pyrene (90 mg, 0.3 mmol) were dissolved in 5 ml of THF:H_2O (4:1). After addition of $CuSO_4 \cdot 5H_2O$ (13 mg, 0.5 mmol) and sodium ascorbate (20 mg, 0.1 mmol), the solution was stirred at room temperature for 24 hours. The experiment was terminated after TLC monitoring, and the solvent was removed. The product **WQ-2** was purified by column chromatography using EtOAc:hexane (1:1).

White solid; mp 118–120 °C; 69% yield; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.25–8.17 (m, 4H, Ar–H), 8.14–8.03 (m, 4H, Ar–H), 7.95 (d, *J* = 7.8 Hz, 1H, Ar–H), 7.81 (d, *J* = 8.9 Hz, 1H, Ar–H), 7.45 (s, 1H, Ar–H), 7.22 (dd, *J* = 8.0 and *J* = 1.4 Hz, 1H, Ar–H), 7,14 (t, *J* = 7.9 Hz, 1H, Ar–H), 7.08 (dd, *J* = 7.7 and *J* = 1.4 Hz, 1H, Ar–H), 6.82 (d, *J* = 8.8 Hz, 1H, Ar–H), 6.25 (s, 2H, CH_2N), 5.39 (s, 2H, CH_2O), 4.42–4.39 (m, 2H, CH_2O), 3.66–3.63 (m, 2H, CH_2O), 3.58–3.55 (m, 2H, CH_2O), 3.50–3.48 (m, 2H, CH_2O), 3.34 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.0, 152.4, 145.2, 138.8, 138.1, 132.1, 131.1, 130.5, 129.3, 129.1, 128.3, 127.7, 127.2, 126.7, 126.4, 126.2, 125.9, 125.8, 125.0, 124.9, 124.4, 123.8, 122.6, 121.9, 120.8, 113.4, 113.4, 71.9, 70.3, 69.5, 64.8, 64.1, 59.0, 52.5. LC-MS/MS. Anal. Calcd. for $C_{42}H_{36}N_4O_4$ $[M+H]^+$: *m/z* 661.2809. Found: *m/z* 661.2822. IR υ_{max} (neat, cm^{-1}): 3424, 3044, 2892, 1732, 1605, 1579, 1508, 1456, 1341, 1267, 1137, 1050, 847, 734.

2.1.3. *Synthesis of* ***WQ-3***

2.1.3.1. *2-((2-hydroxyquinolin-8-yl)oxy)-1-(pyren-1-yl)ethanone,* ***5***

Quinoline-2,8-diol (1.0 mmol), 1-(bromoacetyl)pyrene **4** (323 mg, 1.0 mmol), and K_2CO_3 (276 mg, 2.0 mmol) were dissolved in 25 ml dry THF and were refluxed for 24 hours. The reaction was followed by TLC. The reaction mixture was filtered and the solvent was removed in vacuo. The product **5** was purified by column chromatography using silica gel and EtOAc/hexane (1:2).

Yellow solid; mp 170–173 °C; 75% yield; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.49 (s, 1H, OH), 9.07 (d, *J* = 9.5 Hz, 1H, Ar–H), 8.40 (d, *J* = 8.1 Hz, 1H, Ar–H), 8.31–8.21 (m, 5H, Ar-H), 8.12–8.08 (m, 2H, Ar–H), 7.71 (d, *J* = 9.5 Hz, 1H, Ar–H), 7.20–7.18 (m, 1H, Ar–H), 7.13–7.05 (m, 2H, Ar–H), 6.69–6.66 (m, 1H, Ar–H), 5.64 (s, 2H, CH_2O). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.0, 161.9, 144.2, 140.2, 134.8, 131.0, 130.6, 130.4, 130.4, 127.7, 127.0, 126.8, 126.7, 126.6, 126.1, 125.1, 124.3, 124.0, 123.9, 122.9, 122.0, 120.9, 120.5, 118.0, 112.3, 110.0, 73.1. LC-MS/MS. Anal. Calcd. for $C_{27}H_{17}NO_3$ $[M+H]^+$: m/z 404.1281. Found: m/z 404.1278. IR υ_{max} (neat, cm^{-1}): 3391, 3039, 1654, 1603, 1474, 1253, 1216, 1178, 1103, 839, 796, 730, 625.

2.1.3.2. *2-((2-(2-(2-methoxyethoxy) ethoxy)quinolin-8-yl)oxy)-1-(pyren-1-yl)ethanone,* ***WQ-3***

2-((2-hydroxyquinolin-8-yl)oxy)-1-(pyren-1-yl)ethanone **5** (100 mg, 0.25 mmol) was dissolved in 10 ml of CH_3CN. Then, K_2CO_3 (70 mg, 0.5 mmol) was added and the reaction mixture was refluxed for 30 min. After cooling, 2-(2-methoxyethoxy)ethyl 4-methylbenzenesulfonate (69 mg, 0.25 mmol) was added and the mixture was refluxed overnight. The reaction was terminated after monitoring by TLC and the mixture was filtered. The solvent was removed and the product **WQ-3** was purified by column chromatography using EtOAc:hexane (1:2).

Orange solid; mp 105–108 °C; 70% yield; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.02 (d, *J* = 9.4 Hz, 1H, Ar–H), 8.54 (d, *J* = 8.0 Hz, 1H, Ar–H), 8.26 (dd, *J* = 7.6 and *J* = 2.2 Hz, 2H, Ar–H), 8.23 (d, *J* = 9.4 Hz, 1H, Ar–H), 8.20–8.18 (m, 2H, Ar–H), 8.09–8.07 (m, 2H, Ar–H), 7.95 (d, *J* = 8.9 Hz, 1H, Ar–H), 7.37 (dd, *J* = 8.0 and *J* = 1.3 Hz, 1H, Ar–H), 7.26 (t, *J* = 7.9 Hz, 1H, Ar–H), 7.19 (dd, *J* = 7.7 and *J* = 1.3 Hz, 1H, Ar–H), 6.94 (d, *J* = 8.8 Hz, 1H, Ar–H), 5.72 (s, 2H, CH_2O), 4.50–4.48 (m, 2H, CH_2O), 3.69–3.67 (m, 2H, CH_2O), 3.57–3.55 (m, 2H, CH_2O), 3.48–3.46 (m, 2H, CH_2O), 3.33 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$. 100 MHz): δ 199.4, 161.2, 152.5, 138.9, 138.3, 134.3, 131.0, 130.5, 130.2, 130.0, 129.9, 129.2, 127.1(2), 126.8, 126.5, 126.5, 126.3, 125.0, 124.6, 124.2, 123.8 (2), 121.4, 113.9, 113.7, 74.6, 71.8, 70.3, 69.5, 65.0, 59.0. LC-

MS/MS. Anal. Calcd. for $C_{32}H_{27}NO_5$ $[M+H]^+$: m/z 506.1962. Found: m/z 506.1974. IR υ_{max} (neat, cm^{-1}): 3018, 1694, 1595, 1508, 1481, 1432, 1270, 1215, 1105, 848, 745, 668.

2.1.4. *Synthesis of* ***WQ-4***

2.1.4.1. *(E)-2-(2-(8-(prop-2-yn-1-yloxy)quinolin-2-yl)vinyl)phenol*, **7**

(*E*)-2-(2-hydroxystyryl)quinolin-8-ol **6** (263 mg, 1 mmol) was dissolved in 10 ml of acetone. K_2CO_3 (414 mg, 3 mmol) was added and the reaction mixture was refluxed for 30 min. Then, propargyl bromide (0.24 ml, 2.2 mmol) was added and reflux was continued overnight. The reaction was terminated after TLC monitoring. After the mixture was cooled, it was filtered and the solvent was removed. The product **7** was purified by column chromatography using silica gel and EtOAc/ hexane (1:5).

White solid; 82% yield; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07 (d, *J* = 8.7 Hz, 1H, Ar–H), 8.06 (d, *J* =16.8 Hz, 1H, CH), 7.84 (d, *J* = 8.7 Hz, 1H, Ar–H), 7.79–7.76 (m, 1H, Ar–H), 7.56 (d, *J* = 16.8 Hz, 1H, CH), 7.41 (d, *J* = 0.9 Hz, 1H, Ar–H), 7.40 (s, 1H, Ar–H), 7.32–7.26 (m, 2H, Ar–H), 7.06–7.03 (m, 2H, Ar–H), 5.07 (d, *J* = 2.4 Hz, 2H, CH_2O), 4.80 (d, *J* = 2.4 Hz, 2H, CH_2O), 2.54 (t, *J* = 2.4 Hz, 2H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.9, 155.2, 152.9, 140.2, 136.1, 130.4, 129.5, 128.5, 128.5, 127.1, 126.2, 125.9, 121.9, 120.6, 118.9, 112.8, 110.9, 78.6 (2), 76.1, 75.8, 56.9, 56.3. LC-MS/MS. Anal. Calcd. for $C_{23}H_{17}NO_2$ $[M+H]^+$: *m/z* 340.1332. Found: *m/z* 340.1334.

2.1.4.2. *(E)-2-(2-(2-(2-methoxyethoxy) ethoxy)styryl)-8-(prop-2-yn-1-yloxy)quinoline,* ***8***

(*E*)-2-(2-(8-(prop-2-yn-1-yloxy)quinolin-2-yl)vinyl)phenol **7** (300 mg, 1 mmol) was dissolved in 30 ml of CH_3CN. Next, K_2CO_3 (207 mg, 1.5 mmol) was added and the mixture was stirred under reflux conditions. 2-(2-methoxyethoxy)ethyl-4-methylbenzenesulfonate (274 mg, 1 mmol) was then added and the mixture was stirred under reflux overnight. The reaction was terminated after TLC monitoring and the mixture was filtered. The solvent was removed and the product was purified by column chromatography using EtOAc:hexane (1:2).

Yellow solid; 91 % yield; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06 (d, *J* = 8.6 Hz, 1H, Ar–H), 7.97 (d, *J* = 16.7 Hz, 1H, CH), 7.79–7.75 (m, 2H, Ar–H), 7.51 (d, *J* = 16.7 Hz, 1H, CH), 7.39–7.33 (m, 2H, Ar–H), 7.31–7.27 (m, 1H, Ar–H), 7.09 (dd, *J* = 6.7 and *J* = 2.2 Hz, 1H, Ar–H), 7.06–7.03 (m, 2H, Ar–H), 4.80 (d, *J* = 2.4 Hz, 2H, CH_2O), 4.45 (t, *J* = 5.4 Hz, 2H, CH_2O), 4.10 (t, *J* = 5.4 Hz, 2H, CH_2O), 3.88–3.86 (m, 2H, CH_2O), 3.61–3.59 (m, 2H, CH_2O), 3.38 (s, 3H, OCH_3), 2.56 (t, *J* = 2.4 Hz, 2H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.5, 155.2, 154.5, 140.2, 136.1, 130.3, 129.4, 128.4, 128.2, 127.1, 126.3, 126.2, 121.8, 119.9, 119.2, 112.8, 110.0, 78.6, 75.8, 72.0, 71.0, 69.5, 68.7, 59.1, 59.0, 56.3. LC-MS/MS. Anal. Calcd. for $C_{25}H_{25}NO_4$ $[M+H]^+$: *m/z* 404.1856. Found: *m/z* 404.1862.

2.1.4.3. *(E)-8-((1-(anthracen-9-ylmethyl)-1H-1,2,3-triazol-4-yl)methoxy)-2-(2-(2-(2-methoxyethoxy)ethoxy)styryl)quinoline,* ***WQ-4***

(*E*)-2-(2-(2-(2-methoxyethoxy)ethoxy)styryl)-8-(prop-2-yn-1-yloxy)quinoline **8** (101 mg, 0.25 mmol) and 9-(azidomethyl)anthracene (60 mg, 0.25 mmol) were dissolved in 5 ml of THF:H_2O (4:1). Next, $CuSO_4{\cdot}5H_2O$ (7 mg, 0.25 mmol) and sodium ascorbate (10 mg, 0.05 mmol) were added and the solution was stirred at room temperature for 24 hours. After the experiment was terminated, the solvent was removed. The product **WQ-4** was purified by column chromatography using EtOAc:hexane (2:1).

Yellow solid; mp 144–146 °C; 73 % yield; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.52 (s, 1H, Ar–H), 8.29 (d, *J* = 9.0 Hz, 2H, Ar–H), 8.03–8.01 (m, 2H, Ar–H), 7.96 (d, *J* = 8.6 Hz, 1H, Ar–H), 7.73 (d, *J* = 16.7 Hz, 1H, CH), 7.64 (dd, *J* = 7.7 and *J* = 1.5 Hz, 1H, Ar–H), 7.54–7.36 (m, 9H, Ar–H and CH), 7.21–7.17 (m, 1H, Ar–H), 7.10 (dd, *J* = 6.5 and *J* = 1.5 Hz, 1H, Ar–H), 6.99–6.94 (m, 2H, Ar–H), 6.53 (s, 2H, CH_2N), 5.14 (s, 2H, CH_2O), 4.43 (t, *J* = 5.4 Hz, 2H, CH_2O), 4.06 (t, *J* = 5.4 Hz, 2H, CH_2O), 3.82–3.79 (m, 2H, CH_2O), 3.58–3.55 (m, 2H, CH_2O), 3.36 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.9, 155.5, 154.4, 144.1, 140.0, 136.1, 131.4, 130.7, 130.0, 129.9, 129.6, 129.4, 128.4, 128.4, 127.6, 127.1, 126.2, 125.4, 123.6, 123.0, 122.9, 122.5, 121.6, 119.8, 118.8, 113.3, 110.1, 71.9, 70.9, 69.5, 68.6, 62.8, 59.0, 46.5. LC-MS/MS. Anal. Calcd. for $C_{40}H_{36}N_4O_4$ $[M+H]^+$: *m/z* 637.2817. Found: *m/z* 637.2809. IR υ_{max} (neat, cm^{-1}): 3055, 2933, 2872, 1557, 1452, 1435, 1335, 1245, 1130, 1102, 976, 820, 749, 735.

2.1.5. *Synthesis of* ***WQ-5***

(*E*)-2-(2-(2-(2-methoxyethoxy)ethoxy)styryl)-8-(prop-2-yn-1-yloxy)quinoline **8** (101 mg, 0.25 mmol) and azidomethylpyrene (67 mg, 0.25 mmol)

were dissolved in 5 ml of THF:H_2O (4:1). After the addition of $CuSO_4 \cdot 5H_2O$ (7 mg, 0.25 mmol) and sodium ascorbate (10 mg, 0.05 mmol), the reaction mixture was stirred at room temperature for 24 hours. The reaction was terminated after TLC monitoring and the solvent was removed. The crude product was purified by column chromatography using EtOAc:hexane (1:1).

White solid; mp 114–117 °C; 60 % yield; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24–8.17 (m, 3H, Ar–H), 8.10–7.99 (m, 5H, Ar–H and CH), 7.87 (d, *J* = 7.8 Hz, 1H, Ar–H), 7.79–7.73 (m, 2H, Ar–H), 7.64 (dd, *J* = 7.7 and *J* = 1.5 Hz, 1H, Ar–H), 7.51 (s, 1H, Ar–H), 7.46–7.34 (m, 3H, Ar–H and CH), 7.28 (dd, *J* = 8.2 and *J* = 1.1 Hz, 1H, Ar–H), 7.22–7.18 (m, 1H, Ar–H), 7.06 (dd, *J* = 7.7 and *J* = 1.1 Hz, 1H, Ar–H), 7.01–6.91 (m, 2H, Ar–H), 6.23 (s, 2H, CH_2N), 5.23 (s, 2H, CH_2O), 4.39 (t, *J* = 5.4 Hz, 2H, CH_2O), 4.04 (t, *J* = 5.4 Hz, 2H, CH_2O), 3.79–3.77 (m, 2H, CH_2O), 3.56–3.53 (m, 2H, CH_2O), 3.35 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.9, 155.4, 154.3, 144.5, 136.0, 132.0, 131.1, 130.5, 129.8, 129.6, 129.2, 129.0, 128.7, 128.3, 128.2, 127.5, 127.5, 127.2, 127.2, 126.7, 126.4, 126.1, 125.9, 125.8, 125.0, 124.9, 124.4, 122.9, 121.8, 121.7, 119.8, 118.9, 113.3, 110.0, 71.9, 70.8, 69.5, 68.5, 63.0, 59.0, 52.5. LC-MS/MS. Anal. Calcd. for $C_{42}H_{36}N_4O_4$ $[M+H]^+$: *m/z* 661.2809. Found: *m/z* 661.2822. IR υ_{max} (neat cm^{-1}): 3042, 2873, 2101, 1596, 1556, 1502, 1451, 1329, 1102, 1042, 972, 839, 751, 687.

2.2. *Biology*

2.2.1. *DPPH radical scavenging activity*

A 250 µl aliquot of a DMSO and distilled water solution (19:1) at different concentrations (25–500 µg/ml) were added to the tubes, and 1000 µl of 0.04 % 2,2-diphenyl-1-picrylhydrazyl (DPPH) solution was added. The samples were incubated at 25 °C for 30 minutes. Absorbance was measured at 517 nm using a spectrophotometer. Trolox was used as the positive control.[20]

2.2.2. *Metal chelating activity*

The compound prepared in 500 µl of DMSO and distilled water (19:1) at different concentrations (25–500 µg/ml) was transferred into the tubes, and 1850 µl of methanol and 50 µl of 2mM $FeCl_2$ were added. The mixture was vortexed, and 100 µl of 5mM ferrozine was added to the tubes. After the samples were incubated at room temperature for 10 minutes, absorbance was measured at 562 nm using a spectrophotometer. EDTA was used as positive control.[21]

2.2.3. *Reducing power*

Samples were prepared in DMSO and distilled water (19:1) at test concentrations (25–500 µg/ml) to evaluate their reducing-power activities, and the absorbance of the samples was measured at 700 nm using a spectrophotometer. α-Tocopherol was used as a positive control to compare the activity of the compounds.[22]

2.2.4. *Antibacterial activity*

The antimicrobial activities of the compounds were determined by the disk diffusion method.[23] A total of 20 µl of the compounds prepared at a concentration of 1000 ppm in DMSO and distilled water (19:1) was absorbed onto blank disks and was left to dry. Disks containing sample solution were placed in petri dishes in which bacteria had been cultivated, and the resulting inhibition zones were measured. *Escherichia coli* (ATCC 10536) and *Pseudomonas aeruginosa* (ATCC 9027) were used as Gram-negative bacteria, and *Staphylococcus aureus* (ATCC 6538) and *Enterococcus hirae* (ATCC 10541) were used as Gram-positive bacteria. Ten microgram Imipenem disks were used as the positive control standards.

2.2.5. *DNA binding activity*

Calf thymus DNA (CT-DNA) was used to determine the DNA-binding activities of the samples. For this purpose, 8 µl of the sample (500 µg/ml) solution prepared in DMSO and distilled water (19:1) was transferred into 0.2 ml Eppendorf tubes, and 5 µl of CT-DNA (2 µg/ml) was added. The samples were incubated at 37 °C for 4 hours. Then, the samples were run in a 100 ml volume agarose gel (0.8%) containing 8 µl ethidium bromide (0.05%) for one hour at 80 V, and the resulting gel was photographed under UV light.[24]

2.3. *Structural and electronic analysis*

Geometry optimizations of all the compounds (**WQ-1 – WQ-5**) in this study were performed using the B3LYP/6-311++G(d,p) theoretical method[25] to obtain three-dimensional structures without any symmetry restrictions. Vibrational frequencies and all structural and electronic parameters were obtained using the B3LYP/6-311++G(d,p) approach. Vibrational frequency data

interpretation revealed that, because no negative (imaginary) frequencies were detected, the optimized geometries lay on a minimum on the potential energy surface.

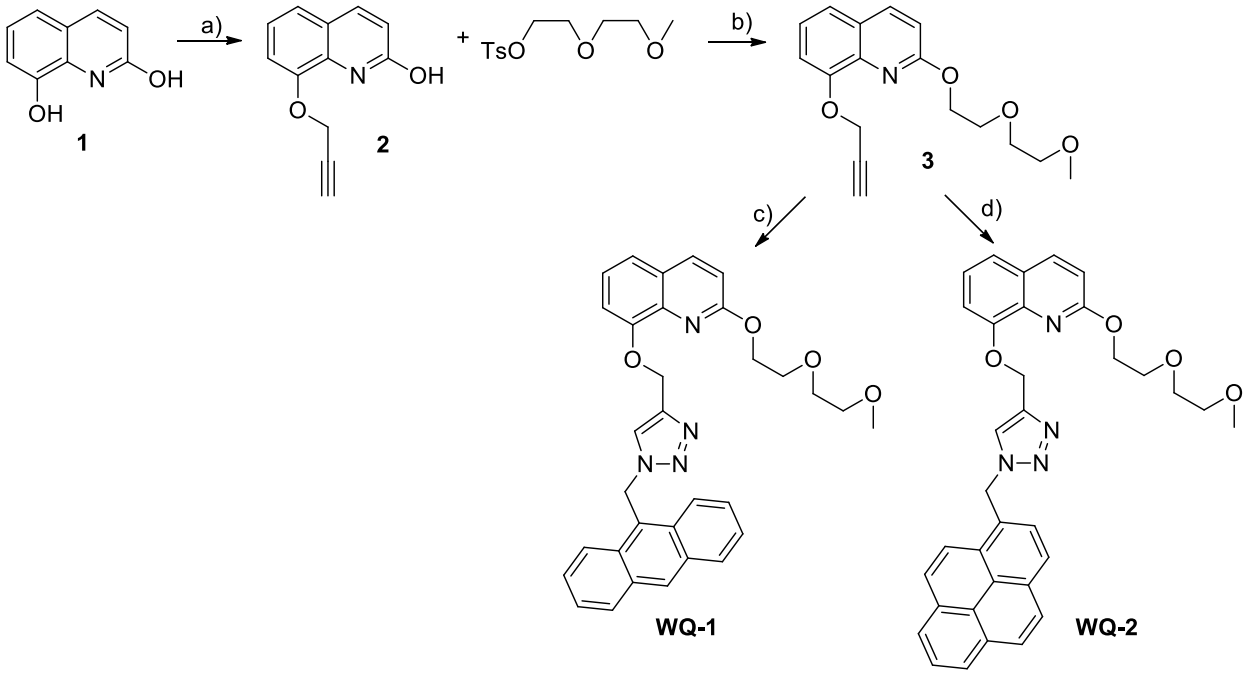
The Gaussian 16W package program was used in conjunction with the GaussView 6 interface to conduct all theoretical calculations.[26]

3. RESULTS AND DISCUSSIONS

3.1. *Chemistry*

New water-soluble quinoline conjugates **WQ-1** and **WQ-2** were synthesized following the procedures outlined in Scheme 1. Quinoline-2,8-diol was used as the key structure for the construction of the target compounds. In the first step, quinoline-2,8-diol was subjected to a monopropagylation reaction with propargyl bromide in the presence of potassium carbonate.

The diglycol monomethyl ether introduced onto the quinoline ring acted as a hydrophilic group to increase water solubility. After the propargylation step, the monopropargylated quinoline derivative was reacted with 2-(2-methoxyethoxy)ethyl 4-methylbenzenesulfonate to obtain the key intermediate **3**. Finally, anthracene and pyrene units were attached to the quinoline derivative, forming a triazole bridge by a copper(I)-mediated click cycloaddition reaction in a 4:1 THF/H_2O solvent mixture, and the target compounds **WQ-1** and **WQ-2** were obtained in high yields. All the new compounds were well characterized by ^1H and ^{13}C NMR and mass spectroscopies.

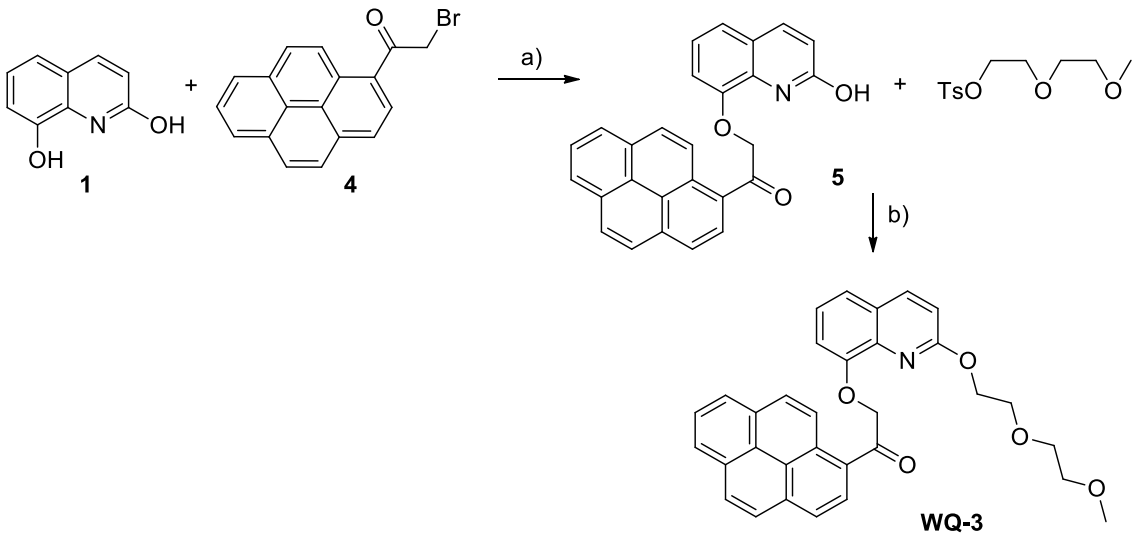


Scheme 1. a) Propargyl bromide, K_2CO_3, acetone; b) K_2CO_3, CH_3CN; c) 9-(azidomethyl)anthracene, $CuSO_4$, sodium ascorbate, THF:H_2O; d) 1-(azidomethyl)pyrene, $CuSO_4$, sodium ascorbate, THF:H_2O

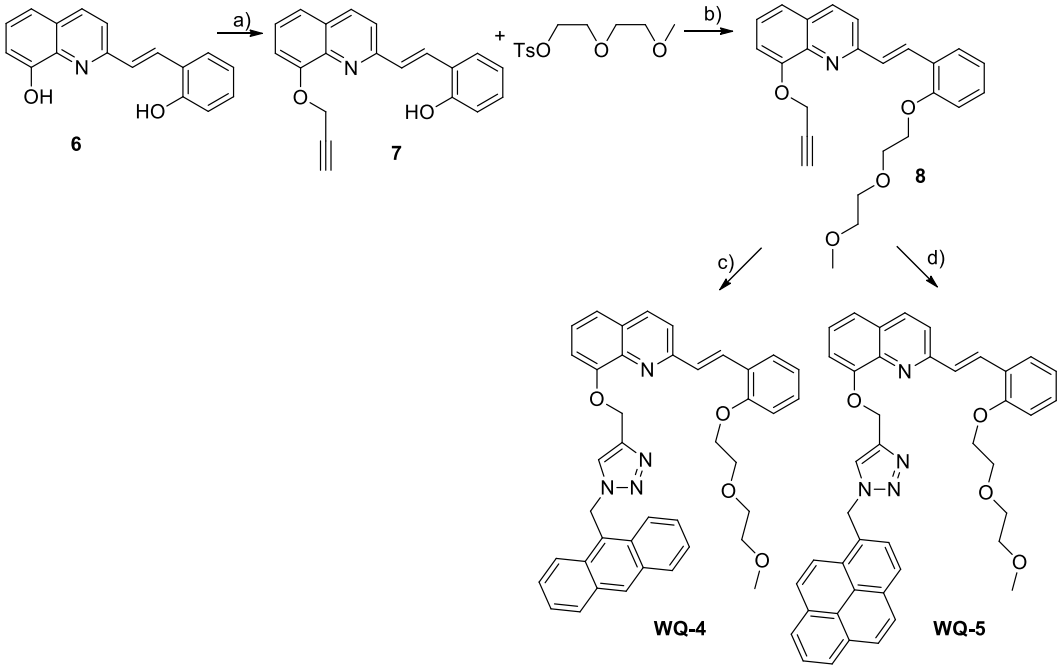
Water-soluble quinoline–pyrene conjugate **WQ-3** was synthesized according to the synthetic route in Scheme 2. The pyrene skeleton was connected to quinoline-2,8-diol in the presence of potassium carbonate through the formation of an acetyl bridge. The water solubility of this derivative was achieved by introducing a diglycol monomethyl ether group to the OH side of the quinoline.

Synthesis of styrylquinoline through the cleavage of two C(sp^3)–H bonds of alkylazaarenes by a green Lewis acid catalyst was conducted according to a previously published method.[27] (E)-2-(2-hydroxystyryl)quinolin-8-ol **6** was used as the template for the construction of **WQ-4** and **WQ-5**.

After the propargylation of the quinoline moiety, the hydrophilic diglycol monomethyl ether group was attached to the styrene moiety according to the reported procedure. Click chemistry was employed for the introduction of the anthracene and pyrene groups to the water-soluble styrylquinoline derivative **8**.



Scheme 2. a) K_2CO_3, THF; b) K_2CO_3, CH_3CN



Scheme 3. a) Propargyl bromide, K_2CO_3, acetone; b) K_2CO_3, CH_3CN; c) 9-(azidomethyl)anthracene, $CuSO_4$, sodium ascorbate, THF:H_2O; d) 1-(azidomethyl)pyrene, $CuSO_4$, sodium ascorbate, THF:H_2O

3.2. *Biology*

3.2.1. *DPPH radical scavenging activity*

The DPPH method was used to determine free radical scavenging capacity as a fast, practical, and economical approach. The method was based on the principle that the dark purple color of the DPPH radical accepts hydrogen from antioxidants in the environment and can be determined quantitatively using a spectrophotometer.[28]

As a result of the study conducted to determine the free radical scavenging activity of the compounds, it was observed that the scavenging activity increased with increasing concentrations of all samples (Fig. 2). At a concentration of 500 µg/ml, the highest activity was shown by **WQ-4** (41.21 ± 1.18 %), **WQ-5** (37.53 ± 1.05 %), **WQ-3** (35.45 ± 1.13 %), **WQ-1** (24.12 ± 0.94 %), and **WQ-2** (18.29 ± 0.72 %), respectively. Trolox, used as the positive standard, exhibited higher activity compared to the samples at all concentrations studied.

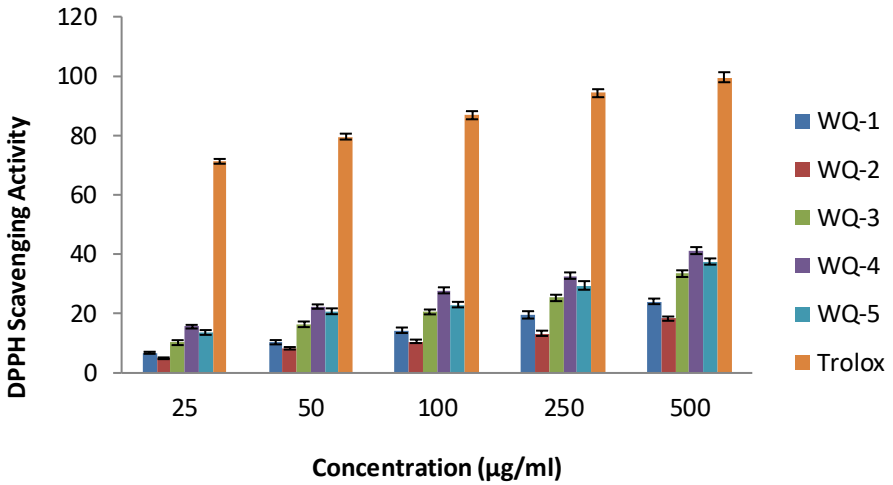


Fig. 2. Radical scavenging activity of the synthesized compounds

3.2.2. *Metal chelating activity*

In living systems, chelating agents reduce free radical formation by providing stability to transition metals and can prevent radical-induced biological damage.[29] It was determined that **WQ-4** and **WQ-5** showed better activity than other compounds, while the remaining compounds showed very low activity. **WQ-5** showed the best chelating activity across all concentration ranges tested, and the activity of this compound at 500 µg/ml was determined to be 23.53 ± 0.97 % (Fig. 3). Even at the lowest concentration tested, 25 µg/ml, the positive control EDTA showed greater than 90 % activity.

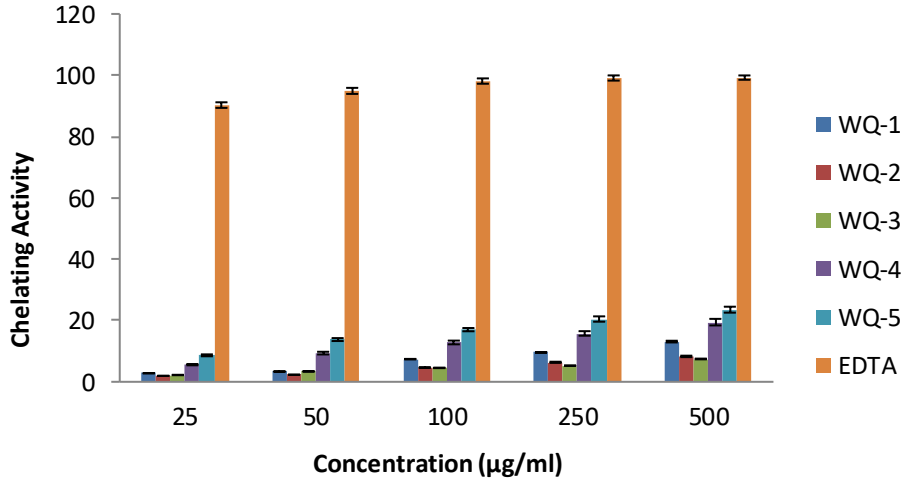


Fig. 3. Metal chelating activity of the synthesized compounds

3.2.3. *Reducing power activity*

Determination of the iron-reducing power capacity of natural or synthesized substances provided an important indicator of their antioxidant properties. This fact was because substances with this activity were electron donors, which played a role in the reduction of oxidative intermediates in lipid peroxidation and were considered potential antioxidants.[30]

The reducing-power activities of all tested compounds increased with concentration (Fig. 4). The activity order of the compounds was determined to be **WQ-4** > **WQ-5** > **WQ-3** > **WQ-2** > **WQ-1** at all studied concentrations. The highest reducing-power activities at 500 µg/ml were observed as 0.417 ± 0.0096 for **WQ-4**, 0.356 ± 0.0077 for **WQ-5**, 0.305 ± 0.0079 for **WQ-3**, 0.216 ± 0.0062 for **WQ-2**, and 0.182 ± 0.0049 for **WQ-1**. The positive standard, α-tocopherol, exhibited higher activity than all compounds, with a value of 0.728 ± 0.0105 at the same concentration.

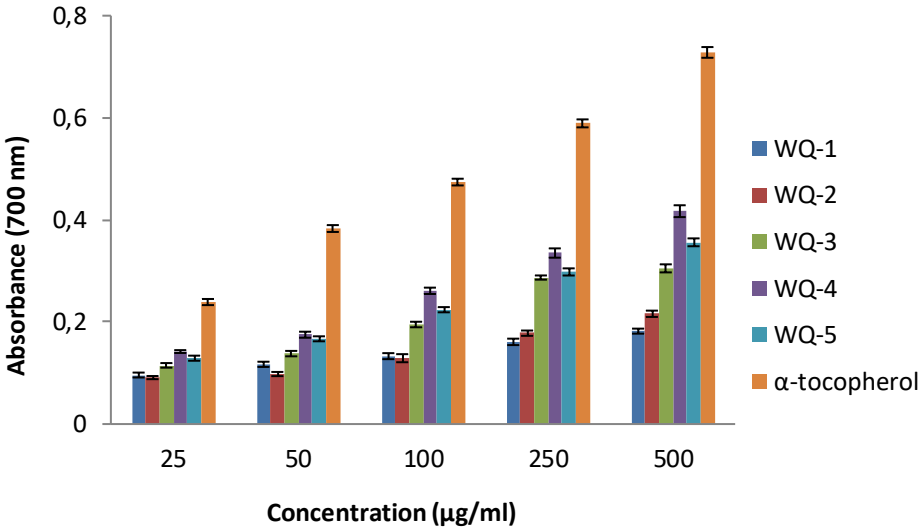


Fig. 4. Reducing power of compounds

3.2.4. *Antibacterial activity*

The antibacterial activity of the newly synthesized compounds was tested using *E. coli*, *P. aeruginosa*, *E. hirae*, and *S. aureus*. In the study, it was observed that only **WQ-3** showed low activity against Gram-positive bacteria, forming an inhibition zone of 8 mm against *E. hirae* and 10 mm against *S. aureus*. The reason why different active compounds were effective against Gram-positive bacteria but ineffective against Gram-negative bacteria may be due to the difference in the permeability of the cell walls of the two bacterial groups.[31]

It was determined that the other compounds studied did not show any activity against the test bacteria. It was also observed that the 10 µg imipenem used as the standard positive control formed an inhibition zone of 31 mm against *E. hirae* and 27 mm against *S. aureus*.

3.2.5. *DNA binding activity*

Agarose gel electrophoresis was used to determine the DNA-binding activity of the compounds. This method was based on the principle that DNA molecules move on the gel according to their mass, charge, and shape, and smaller molecules migrate farther from the starting point. When compounds bind to DNA intercalatively or electrostatically, they reduce the movement of DNA on the gel. As the binding activity increases, the movement on the gel decreases.[32]

The agarose gel electrophoresis results of the newly synthesized compounds are shown in Figure 5. It was determined that all tested compounds moved similarly to the control and did not exhibit any DNA-binding activity.

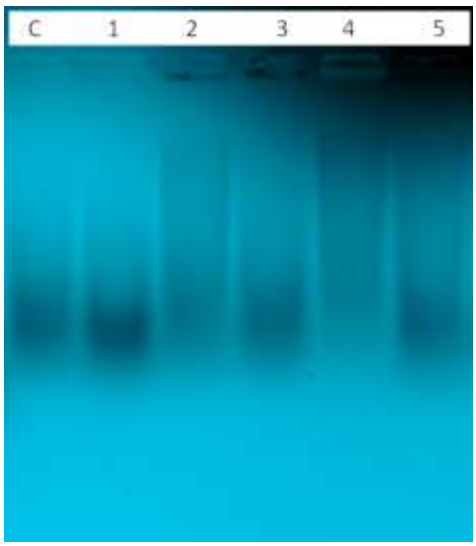


Fig. 5. DNA binding of complexes. Lane C, Control, CT- DNA; Lane 1, CT- DNA + 500 µg/ml of **WQ-1**; Lane 2, CT- DNA + 500 µg/ml of **WQ-2**; Lane 3, CT- DNA + 500 µg/ml of **WQ-3**; Lane 4, CT- DNA + 500 µg/ml of **WQ-4**; Lane 5, CT- DNA + 500 µg/ml of **WQ-5**.

3.3. *Structural and electronic analysis*

Figure 6 displays the three-dimensional geometries of **WQ-1**, **WQ-2**, **WQ-3**, **WQ-4**, and **WQ-5**. It was observed that each triazole moiety in **WQ-1**, **WQ-2**, **WQ-4**, and **WQ-5** was oriented outside of the central cavity, which may have served to reduce interaction with the negative charge created on the nitrogen and two oxygens in the quinoline. The hydroxy styrene and quinoline units formed the highly conjugated planar portion of **WQ-4** and **WQ-5**. It was well known that the triazole unit's three nitrogens carried a significant degree of negativity. All triazole-bearing systems showed the same behavior.

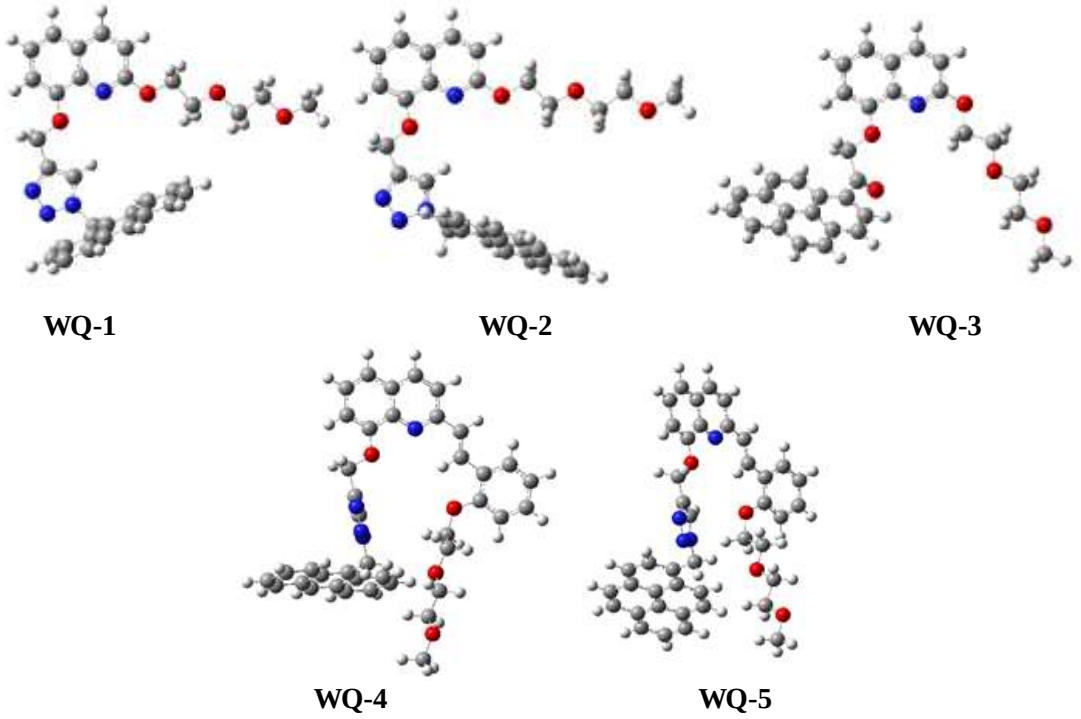


Fig. 6. Optimized geometric structures of **WQ-1**, **WQ-2**, **WQ-3**, **WQ-4**, and **WQ-5**

Molecular electrostatic (MEP) maps provided an excellent representation of the charges found on the constituent parts of the structure. Figure 7 showed a red area denoted as negative charge localization, while a greenish area symbolized positive charge localization. The discussion regarding electron localization on the triazole was nicely represented by the MEPs. Moreover, all five systems possessed negative charge development around the central position, which might have allowed the corresponding system to chelate with cations.

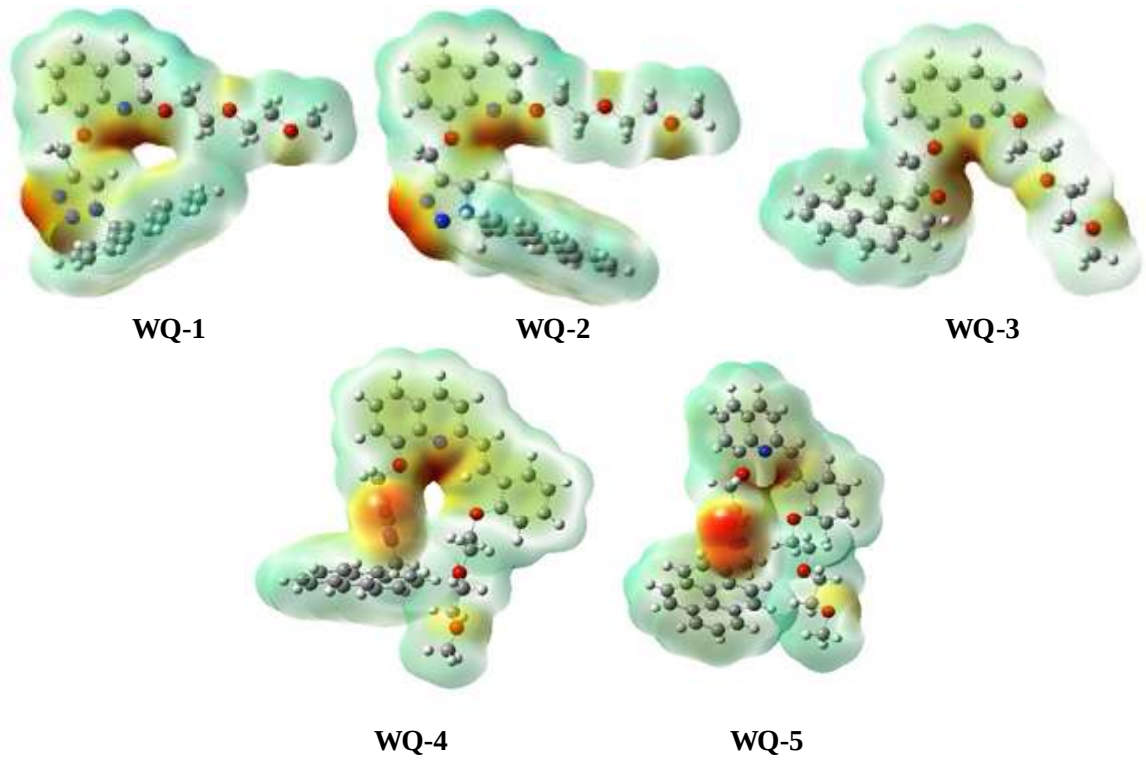


Fig. 7. 3D molecular electrostatic potential maps for **WQ-1**, **WQ-2**, **WQ-3**, **WQ-4**, and **WQ-5**

Computation of frontier orbitals was extremely important for the compounds, as they represented the reactivity centers of the structure. For a molecule, the highest-energy molecular orbital occupied with electrons was called the HOMO (highest occupied molecular orbital), while the lowest-energy empty molecular orbital was called the LUMO (lowest unoccupied molecular orbital). In the present case, both HOMOs and LUMOs were located on the anthracene portion of the molecules for **WQ-1** and **WQ-2**. However, for **WQ-3** and **WQ-4**, quinoline moieties were responsible for the HOMO orbitals, while the LUMOs were located on the pyrenes units. In **WQ-5**, the quinoline portion contributed to both the HOMO and LUMO. Therefore, one could not observe a consistency across the molecules studied herein (Fig. 8).

Computed HOMO energies were found to be –5.20 eV, –5.16 eV, –5.27 eV, –5.26, and –5.30 eV for **WQ-1**, **WQ-2**, **WQ-3**, **WQ-4,** and **WQ-5**, respectively. LUMO energies were computed to be –2.11 eV, –2.16 eV, –2.12 eV, –2.05 eV, and –2.11 eV for **WQ-1**, **WQ-2**, **WQ-3**, **WQ-4**, and **WQ-5**, respectively. The interfrontier molecular orbital energy gap was another important parameter for these molecules, which were close in value across the series under present consideration.

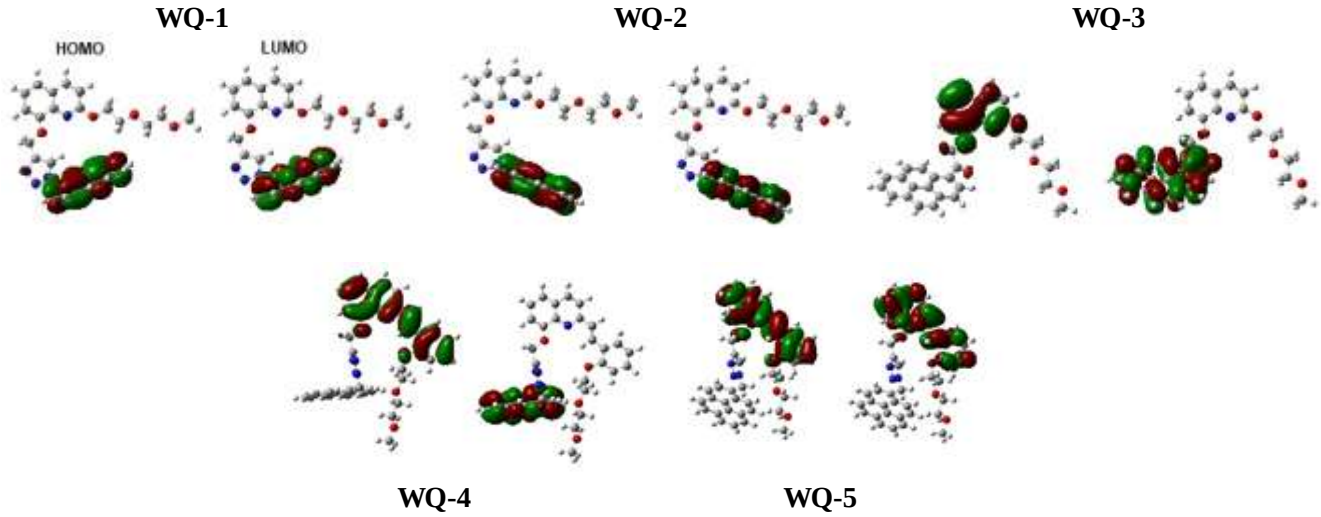


Fig. 8. HOMO and LUMO orbitals of **WQ-1**, **WQ-2**, **WQ-3**, **WQ-4**, and **WQ-5**

4. CONCLUSIONS

In this study, a series of novel, water-soluble quinoline-based conjugates incorporating triazole linkages and anthracene and pyrene units were successfully designed and synthesized in order to explore their biological and electronic properties. The biological activities of the newly synthesized compounds were evaluated. In antioxidant tests conducted for this purpose, it was determined that **WQ-4** showed the best DPPH and reducing-power activity, and **WQ-5** exhibited the highest chelating activity. It was also determined that none of the compounds, except **WQ-3**, showed antibacterial activity, and none of the compounds exhibited DNA-binding capacity.

The electronic and structural properties of the compounds were computed using the B3LYP/6-31++G(d,p) level of theory. The results of these simulations provide insight into potential coordination abilities via cations or reactivities for future studies.

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REFERENCES

(1) Eicher, T.; Hauptmann, S.; Speicher, A., *The Chemistry of Heterocycles* 2nd ed.; Wiley-VCH: Weinheim, **2003**, *6*, 316−336.

(2) Katritzky, A. R.; Ramsden, C. A.; Scriven, E.; Taylor, R. J. K., *Comprehensive Heterocyclic Chemistry III*. **2008**. Elsevier: Oxford, 2008; Vol. 7.

(3) Chen, C. H., Shi, J., Metal chelates as emitting materials for organic electroluminescence. *Coord. Chem. Rev.* **1998**, *171*, 161. https://doi.org/10.1016/S0010-8545(98)90027-3

(4) Kaur, R., Kumar, K., Synthetic and medicinal perspective of quinolines as antiviral agents. *Eur. J. Med. Chem.* **2021**, *215*, 113220. https://doi.org/10.1016/j.ejmech.2021.113220

(5) Keri, R. S., Patil, S. A., Quinoline: A promising antitubercular target. *Biomedicine & Pharmacotherapy* **2014**, *68*, 1161. https://doi.org/10.1016/j.biopha.2014.10.007

(6) Nqoro, X.; Tobeka, N.; Aderibigbe, B. A., Quinoline-based hybrid compounds with antimalarial activity. *Molecules* **2017**, *22*, 2268. https://doi.org/10.3390/molecules22122268

(7) Leatham, P. A.; Bird, H. A.; Wright, V.; Seymour, D.; Gordon, A., A double blind study of antrafenine, naproxen and placebo in osteoarthrosis. *Eur. J. Rheumatol. Inflamm.* **1983**, *6*, 209.

(8) Musiol, R.; Serda, M.; Hensel-Bielowka, S.; Polanski, J., Quinoline-based antifungals. *Curr. Med. Chem.* **2010**, *17*, 1960. https://doi.org/10.2174/092986710791163966

(9) Sun, J., Zhu, H., Yang, Z. M., Zhu, H. L., Synthesis, molecular modeling and biological evaluation of 2-aminomethyl-5-(quinolin-2-yl)-1,3,4-oxadiazole-2(3H)-thione quinolone derivatives as novel anticancer agent. *Eur. J. Med. Chem.* **2013**, *60*, 23. https://doi.org/10.1016/j.ejmech.2012.11.039

(10) Mahamoud, A.; Chevalier, J.; Davin-Regli, A.; Barbe, J.; Pages, J. M., Quinoline derivatives as promising inhibitors of antibiotic efflux pump in multidrug resistant Enterobacter aerogenes isolates. *Curr. Drug Targets* **2006**, *7*, 843. https://doi.org/10.2174/138945006777709557

(11) Muruganantham, N.; Sivakumar, R.; Anbalagan, N.; Gunasekaran, V.; Leonard, J. T., Synthesis, anticonvulsant and antihypertensive activities of 8-substituted quinoline derivatives. *Biol. Pharm. Bull.* **2004**, *27*, 1683. https://doi.org/10.1248/bpb.27.1683

(12) Kamal, A.; Shankaraiah, N.; Devaiah, V.; Reddy, K. L.; Juvekar, A.; Sen, S.; Kurian, N.; Zingde, S., Synthesis of 1,2,3-triazole-linked pyrrolobenzodiazepine conjugates employing 'click' chemistry: DNA-binding affinity and anticancer activity. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1468. https://doi.org/10.1016/j.bmcl.2007.12.063

(13) Chopade, P. K. D.; Shaikh, A. R., Advancements and future perspectives of 1,2,3-triazole scaffold as promising antiviral agent in drug discovery. *Int. J. Pharma Sci. Res.* **2022**, *13*, 4805. https://doi.org/10.13040/IJPSR.0975-8232.13(12).4805-18

(14) Boechat, N.; Ferreira, V. F.; Ferreira, S. B.; Ferreira, M. D. L. G.; Da Silva, F. D. C.; Pinto, A. C.; Krettli, A. U., Novel 1,2,3-triazole derivatives for use against mycobacterium tuberculosis H37Rv (ATCC 27294) strain. *J. Med. Chem.* **2011**, 54, 5988. https://doi.org/10.1021/jm2003624

(15) Gupta, D.; Jain, D. K.; Synthesis, antifungal and antibacterial activity of novel 1,2,4-triazole derivatives. *J. Adv. Pharm. Technol. Res.* **2015**, *6(3)*, 141. https://doi.org/10.4103/2231-4040.161515

(16) Khan, B.; Naiyer, A.; Athar, F.; Ali, S.; Thakur, S. C., Synthesis, characterization and anti-inflammatory activity evaluation of 1,2,4-triazole and its derivatives as a potential scaffold for the synthesis of drugs against prostaglandin-endoperoxide synthase. *Journal of Biomolecular Structure and Dynamics* **2021**, *39(2)*, 457. https://doi.org/10.1080/07391102.2019.1711193

(17) Meldal, M.; Tornøe, C. W., Cu-Catalyzed Azide−Alkyne Cycloaddition. *Chem. Rev.* **2008**, *108*, 2952. https://doi.org/10.1021/cr0783479

(18) Huisgen, R., In *1,3-Dipolar Cycloaddition Chemistry*, Padwa, A., Ed., Wiley, New York, **1984**.

(19) Zhong, K.; Zhou, X.; Hou, R.; Zhou, P.; Hou, S.; Bian, Y.; Zhang, G.; Tang, L.; Shang, X., A water-soluble highly sensitive and selective fluorescent sensor for Hg^{2+} based on 2-(2-(8-hydroxyquinolin)-yl)benzimidazole via ligand-to metal charge transfer (LMCT). *RSC Adv.*, **2014**, *4*, 16612. https://doi.org/10.1039/C4RA00060A

(20) Gümüş, A.; Okumus, V.; Gümüş, S., Synthesis of 2-substituted 8-propargyloxyquinoline derivatives and determination of their antioxidant, antibacterial and DNA binding activities. *Turkish Journal of Chemistry* **2018**, *42*, 1358. https://doi.org/10.3906/kim-1805-77

(21) Baykara, H.; Ilhan, S.; Levent, A.; Seyitoglu, M. S.; Özdemir, S.; Okumuş, V.; Öztomsuk, A.; Cornejo, M., Synthesis, characterization and experimental, theoretical, electrochemical, antioxidant and antibacterial study of a new schiff base and its complexes. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* **2014**, *130*, 270. https://doi.org/10.1016/j.saa.2014.03.094

(22) Ağırtaş, M. S.; Cabir, B.; Özdemir, S.; Okumus, V.; Aslantas, A. Synthesis, aggregation, antioxidant and DNA-binding properties of metallophthalocyanines bearing 5-tert-butyl-2-hydroxyphenoxy groups. *Chemistry Select* **2017**, 2, 11352. https://doi.org/10.1002/slct.201702461

(23) Çelebi, M.; Ağırtaş, M. S.; Okumuş, V.; Özdemir, S., Metallo phthalocyanines bearing (2-((2-hydroxyethyl)(p-tolyl)amino)ethoxy) and (2-((2-phenoxyethyl)(p-tolyl)amino)ethoxy) phthalonitrile substituents: Synthesis, characterization, aggregation behavior, antioxidant and antibacterial activity. *Synthetic Metals* **2014**, *195*, 154. https://doi.org/10.1016/j.synthmet.2014.06.005

(24) Kılıc, A.; Balcı, T. E.; Arslan, N.; Aydemir, M.; Durap, F.; Okumus, V.; Tekin, R., Synthesis of cis-1,2-diol-type chiral ligands and their dioxaborinane derivatives: Application for the asymmetric transfer hydrogenation of various ketones and biological evaluation. *Applied Organometallic Chemistry* **2020**, *34(10)*, 5835. https://doi.org/10.1002/aoc.5835

(25) Becke, A. D., Density-functional exchange-energy approximation with correct asymptotic behavior. *Phys. Rev. A*, **1988**, *38*, 3098. https://doi.org/10.1103/PhysRevA.38.3098

(26) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A.; Jr., Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.;

Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; and Fox, D. J., Gaussian, Inc., Wallingford CT, **2016**.

(27) Gümüş, A.; Gülseven Sıdır, Y.; Sıdır, İ.; Gümüş, S., The solvatochromism and electronic structure of (E)-2-(2-hydroxystyryl)quinolin-8-ol. *Turkish Journal of Chemistry* **2019**, *43*, 1503. https://doi.org/10.3906/kim-1903-36

(28) Ağırtaş, M. S.; Karataş, C.; Gümüş, S.; Okumus, V.; Synthesis of some novel phthalocyanines with methyl 2-(oxy)-2, 2-diphenylacetate substituents, evaluation of their antioxidant- antibacterial activities and electronic properties. *Zeitschrift für anorganische und allgemeine Chemie* **2015**, *641(2)*, 442. https://doi.org/10.1002/zaac.201400445

(29) Gümüş, A.; Okumus, V.; Gümüş, S., Synthesis, biological evaluation of antioxidant-antibacterial activities and computational studies of novel anthracene- and pyrene-based Schiff base derivatives. *Turkish Journal of Chemistry* **2020**, *44*, 1200. https://doi.org/10.3906/kim-2005-61

(30) Tarhan, T.; Dündar, A.; Okumuş, V.; Çulha, M.; Synthesis and characterization of bionanomaterials and evaluation of their antioxidant, antibacterial and DNA cleavage activities. *Chemistry Select.* **2021**, *6* (17), 4217. https://doi.org/10.1002/slct.202004773

(31) Kılıc, A.; Söylemez, R.; Okumuş, V., Design, spectroscopic properties and effects of novel catechol spiroborates derived from Schiff bases in the antioxidant, antibacterial and DNA binding activity. *Journal of Organometallic Chemistry* **2022**, *960*, 122228. https://doi.org/10.1016/j.jorganchem.2021.122228

(32) Kılıç, A.; Alshhab, A.; Okumuş, V., Preparation and spectroscopic properties of bioactive 1, 2, 3-triazole-linked boronate esters for use in antioxidant, antimicrobial, and DNA binding studies. *Journal of Organometallic Chemistry* **2023**, *993*, 122707. https://doi.org/10.1016/j.jorganchem.2023.122707