Biological assessment of substituted quinoline based heteroleptic organometallic compounds

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Supplementary material 1: Experimental section

1. Materials and methods

1.1 Materials and reagents

All the chemicals and solvents were of reagent grade and used as purchased; double distilled water was used throughout the studies. Pentamethylcyclopentadienyl ruthenium(III) chloride [{(Cp*)Ru(μ-Cl)Cl}$_2$], 2-acetyl pyridine, 2-acetyl thiophene, 2-aminobenzophenon, 2-amino-5-chlorobenzophenon, 2-amino-2', 5-dichlorobenzophenon, 2-amino-5-chloro-2'-fluoro-benzophenon, HS DNA and ethylenediaminetetraacetic acid disodium salt (edta) were purchased from Sigma Aldrich Chemical Co. (India). Agarose, Luria Broth (LB), ethidium bromide (EtBr), tris-acetyl-edta (TAE), bromophenol blue and xylene cyanol FF were purchased from Himedia (India). *S. pombe* Var. Paul Linder 3360 was obtained from IMTECH, Chandigarh.

1.2 Physical measurements

Precoated silica gel plates (silica gel 0.25 mm, 60 G F 254; Merck, Germany) were used for thin layer chromatography. The LC-MS spectra were recorded using make waters model micromass quattro micro API mass spectrometer. The electronic spectra were recorded on a UV–160A UV–Vis spectrophotometer, Shimadzu, Kyoto (Japan). The ^{1}H NMR and ^{13}C NMR were recorded with a Bruker Avance (400 MHz). Photo quantization of the gel after electrophoresis was done using AlphaDigiDoc™ RT. Version V.4.0.0 PC-Image software, California (USA). IR spectra were recorded on a FT–IR Shimadzu spectrophotometer with sample prepared as KBr pellets in the range 4000–400 cm^{-1}. C, H,

and N elemental analyses were performed using thermofinnigan at CHN Lab, Panjab University, Chandigarh. Melting points (°C, uncorrected) were determined in open capillaries on ThermoCal$_{10}$ melting point apparatus (Analab Scientific Pvt. Ltd, India). The magnetic moments were measured by Gouy's method using mercury tetrathiocyanatocobaltate(II) as the calibrant ($\chi_g = 16.44 \times 10^{-6}$ cgs units at 20 °C), Citizen balance. Conductance measurement was carried out using conductivity meter model number E–660A. The thermo gram of complexes was recorded with a Mettler Toledo TGA/DSC 1 thermo gravimetric analyser. Antibacterial study was carried out by means of laminar air flow cabinet Toshiba, Delhi (India).

2. General method for synthesis of quinoline ligands (3a-3g)

To the solution of appropriate β-amino carbonyl compound i.e. 2-aminobenzophenon (1a), 2-amino-5-chlorobenzophenon (1b), 2-amino-2', 5-dichlorobenzophenon (1c), 2-amino-5-chloro-2'-fluoro-benzophenon (1d) (6 mmol) in 10 mL of methanol, 2-acetyl pyridine (2a) (6 mmol, 0.67 mL) or 2-acetyl thiophene (2b) (6 mmol, 0.65 mL) and sodium methoxide (6 mmol) were added and the reaction mixture was refluxed for 5–6 h. Conversion was monitored in every 60 minutes interval on precoated silica TLC plates by using mixture of ethyl acetate and hexane as mobile phase. The excess of solvent was removed under reduced pressure and the reaction mixture was cooled on an ice bath. The products precipitated out at low temperature were washed five times with 60 mL distilled water, reconstituted in minimum amount of methanol and dried under reduced pressure.

2.1 Synthesis of 4-phenyl-2-(pyridin-2-yl) quinoline (3a) (L^1)

Prepared by above method using 2-aminobenzophenon **(1a)** (6 mmol, 1.18 g) and 2-acetyl pyridine **(2a)** (6 mmol, 0.67 mL) after 5–6 h reflux; **Yield:** 65%; **Color:** white amorphous solid; **Mp:** 152 °C; **Mol. wt.** 282.35 g/mol; **Empirical formula**: $C_{20}H_{14}N_2$, **Calc. (found) (%):** C, 85.08 (85.02); H, 5.00 (4.96); N, 9.92 (9.97); **Mass spectra (m/z %):** 283 (100) [M+]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.346-8.757 (aromatic 14H, m) **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 156.38 ($C_{1''}$), 155.65 (C_4), 149.29 (C_2), 149.20 ($C_{5''}$), 148.53 (C_{10}), 138.40 ($C_{1'}$), 136.97 ($C_{3''}$), 130.62 (C_8), 130.25 (C_7), 129.71 ($C_{3', 5'}$), 129.45 ($C_{4'}$), 128.51 ($C_{2', 6'}$), 126.83 (C_9), 126.79 (C_6), 125.85 (C_5), 124.08 ($C_{4''}$), 121.90 ($C_{2''}$), 119.28 (C_3); [Signals observed=18: Ar-C=6, Ar-CH=12]; **IR (KBr, 4000–400 cm^{-1}):** 3061, ν(C–H)$_{\text{ar stretching}}$; 1588, ν(C=N); 1444, ν(C=C); 796, ν(C–H)$_{\text{ar bending}}$.

2.2 Synthesis of 6-chloro-4-phenyl-2-(pyridin-2-yl) quinoline (3b) (L^2)

Prepared by above method using 2-amino-5-chlorobenzophenon **(1b)** (6 mmol, 1.39 g) and 2-acetyl pyridine **(2a)** (6 mmol, 0.67 mL) after 5–6 h reflux; **Yield:** 63%; **Color:** white amorphous solid; **Mp:** 148 °C; **Mol. wt.** 316.79 g/mol; **Empirical formula**: $C_{20}H_{13}N_2Cl$, **Calc. (found) (%):** C, 75.83 (75.80); H, 4.14 (4.19); N, 8.84 (8.79); **Mass spectra (m/z %):** 317 (100) [M+], 319 [M+2]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.380-8.754 (aromatic 13H, m); **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 155.97 ($C_{1''}$),

155.88 (C_2), 149.25 ($C_{5''}$), 148.56 (C_4), 146.90 (C_{10}), 137.73 ($C_{1'}$), 137.03 ($C_{3''}$), 132.73 (C_6), 131.79 (C_5), 130.38 ($C_{3', 5'}$), 129.56 ($C_{4'}$), 128.71 (C_7), 128.63 (C_8), 127.49 (C_9), 124.69 ($C_{2', 6'}$), 124.26 ($C_{4''}$), 121.85 ($C_{2''}$), 120.02 (C_3); [Signals observed=18: Ar-C=7, Ar-CH=11]; **IR (KBr, 4000–400 cm^{-1}):** 3054, ν(C–H)$_{ar\ stretching}$; 1591, ν(C=N); 1381, ν(C=C); 1072, ν(C–Cl); 787, ν(C–H)$_{ar\ bending}$.

2.3 Synthesis of 6-chloro-4-(2-chlorophenyl)-2-(pyridin-2-yl) quinoline (3c) (L^3)

Prepared by above method using 2-amino-2', 5-dichlorobenzophenon **(1c)** (6 mmol, 1.59 g) and 2-acetyl pyridine **(2a)** (6 mmol, 0.67 mL) after 5–6 h reflux; **Yield:** 67%; **Color:** white amorphous solid; Mp: 151 °C; **Mol. wt.** 351.23 g/mol; **Empirical formula**: $C_{20}H_{12}N_2Cl_2$, **Calc. (found) (%):** C, 68.39 (68.32); H, 3.44 (3.40); N, 7.98 (7.92); **Mass spectra (m/z %):** 351 (100) [M+], 353 [M+2], 355 [M+4]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.384-8.742 (aromatic 12H, m); **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 155.25 ($C_{1''}$), 154.06 (C_2), 152.67 (C_4), 149.26 ($C_{5''}$), 145.96 (C_{10}), 137.07 ($C_{3''}$), 136.26 ($C_{1'}$), 135.27 (C_6), 134.47 ($C_{2'}$), 131.77 ($C_{4'}$), 131.42 ($C_{3'}$), 130.57 (C_5), 130.06 (C_8), 129.92 (C_7), 126.96 ($C_{6'}$), 124.61 ($C_{5'}$), 124.34 ($C_{4''}$), 121.88 ($C_{2''}$), 120.53 (C_3), 119.83 (C_9); [Signals observed=20: Ar-C=8, Ar-CH=12]; **IR (KBr, 4000–400 cm^{-1}):** 3061, ν(C–H)$_{ar\ stretching}$; 1591, ν(C=N); 1473, ν(C=C); 1057, ν(C–Cl); 794, ν(C–H)$_{ar\ bending}$.

2.4 Synthesis of 6-chloro-4-(2-fluorophenyl)-2-(pyridin-2-yl) quinoline (3d) (L^4)

Prepared by above method using 2-amino-5-chloro-2'-fluoro-benzophenon **(1d)** (6 mmol, 1.5 g) and 2-acetyl pyridine **(2a)** (6 mmol, 0.67 mL) after 5–6 h reflux; **Yield:** 68%; **Color:** white amorphous solid; **Mp:** 155 °C; **Mol. wt.** 334.78 g/mol; **Empirical formula**: $C_{20}H_{12}N_2FCl$, **Calc. (found) (%):** C, 71.75 (71.70); H, 3.61 (3.55); N, 8.37 (8.42); **Mass spectra (m/z %):** 335 (100) [M+], 337 [M+2]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.299-8.746 (aromatic 12H, m); **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 160.20 ($C_{2'}$), 157.58 ($C_{1''}$), 155.23 (C_2), 152.87 (C_4), 149.23 ($C_{5''}$), 147.73 (C_{10}), 137.03 ($C_{3''}$), 136.37 ($C_{1'}$), 135.78 (C_6), 131.70 ($C_{4'}$), 130.82 ($C_{6'}$), 130.74 (C_5), 130.53 (C_8), 124.52 (C_7), 124.30 ($C_{5'}$), 121.85 ($C_{4''}$), 120.92 ($C_{2''}$), 119.81 (C_9), 116.21 ($C_{3'}$), 115.99 (C_3); [Signals observed=20: Ar-C=8, Ar-CH=12]; **IR (KBr, 4000–400 cm^{-1}):** 3056, ν(C–H)$_{ar\ stretching}$; 1588, ν(C=N); 1356, ν(C=C); 1202, ν(C–F); 1072, ν(C–Cl); 764, ν(C–H)$_{ar\ bending}$.

2.5 Synthesis of 4-phenyl-2-(thiophen-2-yl) quinoline (3e) (L^5)

Prepared by above method using 2-aminobenzophenon **(1a)** (6 mmol, 1.18 g) and 2-acetyl thiophene **(2b)** (6 mmol, 0.65 mL) after 5–6 h reflux; **Yield:** 65%; **Color:** white amorphous solid; **Mp:** 165 °C; **Mol. wt.** 287.38 g/mol; **Empirical formula**: $C_{19}H_{13}NS$, **Calc. (found) (%):** C, 79.41 (79.37); H, 4.56 (4.51); N, 4.87 (4.80); **Mass spectra (m/z %):** 288 (100) [M+]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.172-8.204 (aromatic 13H, m); **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 158.90 (C_2), 151.89 (C_4), 149.08 (C_{10}), 148.66 ($C_{1''}$), 145.42 ($C_{1'}$), 138.20 (C_9), 129.98 (C_8), 129.68 (C_7), 129.53 ($C_{3', 5'}$), 128.63 ($C_{4'}$), 128.58 ($C_{2', 6'}$), 128.49 ($C_{4''}$), 128.09 ($C_{3''}$), 126.15 ($C_{2''}$), 125.92 (C_6), 125.70 (C_5), 117.93 (C_3); [Signals observed=17: Ar-C=6, Ar-CH=11]; **IR (KBr, 4000–400 cm^{-1}):** 3056, ν(C–H)$_{ar\ stretching}$; 1588, ν(C=N); 1357, ν(C=C); 1242, ν(C–S); 772, ν(C–H)$_{ar\ bending}$.

2.6 Synthesis of 6-chloro-4-phenyl-2-(thiophen-2-yl) quinoline (3f) (L^6)

Prepared by above method using 2-amino-5-chlorobenzophenon **(1b)** (6 mmol, 1.39 g) and 2-acetyl thiophene **(2b)** (6 mmol, 0.65 mL) after 5–6 h reflux; **Yield:** 62%; **Color:** white amorphous solid; **Mp:** 160 °C; **Mol. wt.** 321.82 g/mol; **Empirical formula**: $C_{19}H_{12}NClS$, **Calc. (found) (%):** C, 70.91 (70.83); H, 3.76 (3.70); N, 4.35 (4.29); **Mass spectra (m/z %):** 322 (100) [M+], 324 [M+2]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.168-8.115 (aromatic 12H, m); **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 152.12 (C_2), 148.32 (C_4), 147.08 (C_{10}), 144.98 ($C_{1''}$), 137.54 ($C_{1'}$), 131.99 (C_6), 131.23 (C_5), 130.54 (C_8), 129.38 ($C_{3',5'}$), 128.88 ($C_{4'}$), 128.83 ($C_{2',6'}$), 128.76 ($C_{4''}$), 128.14 (C_7), 126.58 (C_9), 126.16 ($C_{3''}$), 124.56 ($C_{2''}$), 118.62 (C_3); [Signals observed=17: Ar-C=7, Ar-CH=10]; **IR (KBr, 4000–400 cm^{-1}):** 3071, ν(C–H)$_{ar\ stretching}$; 1588, ν(C=N); 1356, ν(C=C); 1234, ν(C–S); 1027, ν(C–Cl); 772, ν(C–H)$_{ar\ bending}$.

2.7 Synthesis of 6-chloro-4-(2-fluorophenyl)-2-(thiophen-2-yl) quinoline (3g) (L^7)

Prepared by above method using 2-amino-5-chloro-2'-fluoro-benzophenon **(1d)** (6 mmol, 1.5 g) and 2-acetyl thiophene **(2b)** (6 mmol, 0.65 mL) after 5–6 h reflux; **Yield:** 63%; **Color:** white amorphous solid; **Mp:** 162 °C; **Mol. wt.** 339.81 g/mol; **Empirical formula**: $C_{19}H_{11}NFClS$, **Calc. (found) (%):** C, 67.16 (67.11); H, 3.26 (3.20); N, 4.12 (4.17); **Mass spectra (m/z %):** 340 (100) [M+], 342 [M+2]; **^{1}H NMR (400 MHz, $CDCl_3$-d_1) δ/ppm:** 7.167-8.148 (aromatic 11H, m); **^{13}C NMR (100 MHz, $CDCl_3$-d_1) δ/ppm:** 160.86 (C_2), 158.39 ($C_{2'}$), 152.09 (C_4), 146.84 (C_{10}), 144.82 ($C_{1''}$), 142.41 ($C_{1'}$), 132.18 (C_6), 131.22 ($C_{4'}$), 130.95 ($C_{6'}$), 130.87 (C_5), 130.71 (C_8), 129.01 (C_7), 128.16 ($C_{4''}$), 126.67 (C_9), 126.27 ($C_{3''}$), 124.57 ($C_{2''}$), 124.54 ($C_{5'}$), 119.56 ($C_{3'}$), 116.38 (C_3); [Signals observed=19: Ar-C=8, Ar-CH=11]; **IR (KBr, 4000–400 cm^{-1}):** 3071, ν(C–H)$_{ar\ stretching}$; 1596, ν(C=N); 1356, ν(C=C); 1242, ν(C–S); 1157, ν(C–F); 1069, ν(C–Cl); 756, ν(C–H)$_{ar\ bending}$.

2.4. General synthesis of the complexes

An organometallic half-sandwich Ru(III) metal complexes **(5a-5g)** of the general formula [(Cp*)Ru(L^n)Cl]•Cl were synthesized by the reactions of [{(Cp*)Ru(μ-Cl)Cl} with the respective ligands **(3a-3g)** in a 1:2 molar ratio of dichloromethane and methanol, respectively.

2.4.1 Synthesis of [(Cp*)Ru(L^1)Cl]• Cl (5a)

Dichloromethane and methanolic suspension of the precursor of [{(Cp*)Ru(μ-Cl)Cl}(($_2$] (0.309 g, 0.5 mmol) was refluxed for 10 minutes. Then a solution of ligand (**3a)** (0.282 g, 1.0 mmol in 20 mL dichloromethane), was added and the reaction was stirred yielding a red-brown solution. The resulting mixture was stirred at room temperature for 16 h. Then the solution was filtered through celite in order to remove solid particles and the solvent was removed under reduced pressure. The residue was dissolved in methanol (5 mL), and the product was precipitated by addition of diethyl ether (30 mL), isolated by filtration and dried in vacuo to obtain the complex. The complex is soluble in methanol, ethanol, dichloromethane, acetonitrile, dimethylformamide and dimethyl sulphoxide but insoluble in petroleum ether and diethyl ether. The proposed reaction for the synthesis of complexes (**5a-5g)** is shown in scheme 1. **Yield:** 68%; **Mp:** ≥ 300 °C; **μ_{eff}:** 2.20 BM; **Mol.**

wt. 589.55 g/mol; **Empirical formula** :$C_{30}H_{29}N_2Cl_2Ru$, **Calc. (found) (%):** C, 61.12 (61.05); H, 4.96 (4.91); N, 4.75 (4.78); Ru, 17.14 (17.07); **IR (KBr, 4000–400 cm^{-1}):** 3054, ν(C–H)$_{ar\ stretching}$; 2925, ν(C–H)$_{al\ stretching}$; 1598, ν(C=N); 1473, ν(C=C); 787, ν(C–H)$_{ar\ bending}$; **Conductance:** 42 cm^2 Ω^{-1} mol^{-1}; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 360 (12856), 348 (13255), 291 (13452).

2.4.2 Synthesis of [(Cp*)Ru(L^2)Cl]• Cl (5b)

It was synthesized using ligand (**3b)** (0.316 g, 1.0 mmol). **Yield:** 70%; **Mp:** ≥ 300 °C; **μ$_{eff}$:** 2.23 BM; **Mol. wt.** 623.99 g/mol; **Empirical formula** :$C_{30}H_{28}N_2Cl_3Ru$, **Calc. (found) (%):** C, 57.75 (57.70); H, 4.52 (4.55); N, 4.49 (4.42); Ru, 16.20 (16.13); **IR (KBr, 4000–400 cm^{-1}):** 3071, ν(C–H)$_{ar\ stretching}$; 2933, ν(C–H)$_{al\ stretching}$; 1603, ν(C=N); 1372, ν(C=C); 1088, ν(C–Cl); 788, ν(C–H)$_{ar\ bending}$; **Conductance:** 46 cm^2 Ω^{-1} mol^{-1}; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 370 (13112), 351 (13850), 285 (23460).

2.4.3 Synthesis of [(Cp*)Ru(L^3)Cl]• Cl (5c)

It was synthesized using ligand (**3c)** (0.351 g, 1.0 mmol). **Yield:** 69%; **Mp:** ≥ 300 °C; **μ$_{eff}$:** 2.17 BM; **Mol. wt.** 658.43 g/mol; **Empirical formula** :$C_{30}H_{27}N_2Cl_4Ru$, **Calc. (found) (%):** C, 54.73 (54.70); H, 4.13 (4.08); N, 4.25 (4.20); Ru, 15.35 (15.31); **IR (KBr, 4000–400 cm^{-1}):** 3055, ν(C–H)$_{ar\ stretching}$; 2976, ν(C–H)$_{al\ stretching}$; 1588, ν(C=N); 1473, ν(C=C); 1088, ν(C–Cl); 772, ν(C–H)$_{ar\ bending}$; **Conductance:** 39 cm^2 Ω^{-1} mol^{-1}; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 366 (13332), 347 (14233), 289 (24565).

2.4.4 Synthesis of [(Cp*)Ru(L^4)Cl]• Cl (5d)

It was synthesized using ligand (**3d)** (0.334 g, 1.0 mmol). **Yield:** 70%; **Mp:** ≥ 300 °C; **μ$_{eff}$:** 2.18 BM; **Mol. wt.** 641.98 g/mol; **Empirical formula** :$C_{30}H_{27}N_2FCl_3Ru$, **Calc. (found) (%):** C, 56.13 (56.08); H, 4.24 (4.20); N, 4.36 (4.32); Ru, 15.74 (15.67); **IR (KBr, 4000–400 cm^{-1}):** 3076, ν(C–H)$_{ar\ stretching}$; 2945, ν(C–H)$_{al\ stretching}$; 1585, ν(C=N); 1351, ν(C=C); 1206, ν(C–F); 1094, ν(C–Cl); 787, ν(C–H)$_{ar\ bending}$; **Conductance:** 58 cm^2 Ω^{-1} mol^{-1}; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 358 (12955), 345 (14230), 288 (13150).

2.4.5 Synthesis of [(Cp*)Ru(L^5)Cl]• Cl (5e)

It was synthesized using ligand (**3e)** (0.287 g, 1.0 mmol). **Yield:** 72%; **Mp:** ≥ 300 °C; **μ$_{eff}$:** 2.20 BM; **Mol. wt.** 594.58 g/mol; **Empirical formula** :$C_{29}H_{28}NCl_2SRu$, **Calc. (found) (%):** C, 58.58 (58.52); H, 4.75 (4.71); N, 2.36 (2.32); Ru, 17.00 (16.93); **IR (KBr, 4000–400 cm^{-1}):** 3068, ν(C–H)$_{ar\ stretching}$; 2933, ν(C–H)$_{al\ stretching}$; 1602, ν(C=N); 1377, ν(C=C); 1257, ν(C–S); 780, ν(C–H)$_{ar\ bending}$; **Conductance:** 56 cm^2 Ω^{-1} mol^{-1}; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 362 (13546), 350 (14233), 292 (24215).

2.4.6 Synthesis of [(Cp*)Ru(L^6)Cl]• Cl (5f)

It was synthesized using ligand (**3f)** (0.321 g, 1.0 mmol). **Yield:** 68%; **Mp:** ≥ 300 °C; **μ$_{eff}$:** 2.22 BM; **Mol. wt.** 629.02 g/mol; **Empirical formula** :$C_{29}H_{27}NCl_3SRu$, **Calc. (found) (%):** C, 55.37 (55.32); H, 4.33 (4.28); N, 2.23 (2.26); Ru, 16.07 (16.01); **IR (KBr, 4000–400 cm^{-1}):** 3082, ν(C–H)$_{ar\ stretching}$; 2923, ν(C–H)$_{al\ stretching}$; 1591, ν(C=N); 1359, ν(C=C); 1242, ν(C–S); 1057, ν(C–Cl); 777, ν(C–H)$_{ar\ bending}$; **Conductance:** 63 cm^2 Ω^{-1} mol^{-1}; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 364 (13122), 347 (14210), 290 (24354).

2.4.7 Synthesis of [(Cp*)Ru(L^7)Cl]• Cl (5g)

It was synthesized using ligand (**3g)** (0.339 g, 1.0 mmol). **Yield:** 72%; **Mp:** ≥ 300 °C; **μ_{eff}:** 2.15 BM; **Mol. wt.** 647.01 g/mol; **Empirical formula** :$C_{29}H_{26}NFCl_3SRu$, **Calc. (Found) (%):** C, 53.83 (53.77); H, 4.05 (4.01); N, 2.16 (2.11); Ru, 15.62 (15.69); **IR (KBr, 4000–400 cm^{-1}):** 3056, ν(C–H)$_{ar\ stretching}$; 2923, ν(C–H)$_{al\ stretching}$; 1582, ν(C=N); 1383, ν(C=C); 1279, ν(C–S); 1162, ν(C–F); 1096, ν(C–Cl); 758, ν(C–H)$_{ar\ bending}$; **Conductance:** 67 $cm^2\ \Omega^{-1}\ mol^{-1}$; **UV-Vis: λ (nm) (ε, L mol^{-1} cm^{-1}):** 365 (12854), 348 (13856), 292 (23775).

3. Biological applications of synthesized compounds

3.1 Cellular level bioassay using *S. pombe* cells

Cellular level bioassay was done using *S. pombe* cells, which were grown in liquid yeast extract media in 150 mL Erlenmeyer flask containing 50 mL of yeast extract media. Flask was incubated at 30 °C on shaker at 150 rpm till the exponential growth of *S. pombe* obtained (24 to 30 h). Then the cell culture was treated with the different concentrations (2, 4, 6, 8, 10 mg/L) of synthesized complexes, free ligands and also with dimethylsulphoxide (DMSO) as a control and further allowed to grow for 16-18 h. Next day, by centrifugation at 10,000 rpm 10 mintunes; treated cells were collected and dissolved in 500 µL of PBS. The 80 µL of yeast culture dissolved in PBS and 20 µL of 0.4% trypan blue prepared in PBS were mixed and cells were observed in a compound microscope (40X). The dye could enter the dead cell only so they appeared blue whereas live cells resisted the entry of dye. The number of dead cells and number of live cells were counted in one field. Cell counting was repeated in two more of the microscopic fields and average percentage of cells died due to synthesized compounds were calculated.

3.2 *In vitro* brine shrimp lethality bioassay (BSLB)

Brine shrimp (Artemia cysts) eggs were hatched in a shallow rectangular plastic dish (22×32 cm), filled with artificial seawater, which was prepared with commercial salt mixture and double distilled water. An unequal partition was made in the plastic dish with the help of a perforated device. Approximately 50 mg of eggs were sprinkled into the large compartment and was opened to ordinary light. After two days, nauplii were collected by a pipette from the lighted side. The detail experimental process is reported in newly published literatures.[1, 2]

3.3. *In vitro* antimicrobial study

The *in vitro* antimicrobial activities of free ligands, and ruthenium complexes were tested against two gram positive; Staphylococcus aureus, Bacillus subtilis and three gram negative; Serratia marcescens, Escherichia coli, Pseudomonas aeruginosa, microorganisms. The MIC value was determined by broth dilution technique.[3] The detail experimental process is reported in literatures.[1, 2]

3.4 DNA interactions

(I) By absorption spectral analysis

DNA-mediated hypochromic and bathochromic shifts under the influence of the ruthenium complexes were measured with the help of UV–Visible absorbance spectra. UV–Visible spectral titration of Ru(III) complexes (in DMSO) with HS–DNA in phosphate buffer was carried out to inspect the binding mode for the complexes. The concentration of HS DNA was determined by measuring absorbance at 260 nm and using 12858 L mol^{-1} cm^{-1} as the molar extinction coefficient value.[4] In experiment, fixed amount of DNA solution (100 µL) in phosphate buffer was added to sample cell holding in definite concentration of complex solution (20 µmol L^{-1}) and reference cell to nullify the effect of HS DNA, and allowed to incubate for 10 min prior to the spectra being recorded. DMSO was also added into the reference cell as a control to nullify the effect of DMSO. The intrinsic binding constant, K_b, was determined by published literatures.[1, 2]

(II) By hydrodynamic volume or viscosity measurement

An Ubbelohde viscometer maintained at a constant temperature of 27±0.1 °C in a thermostatic jacket, was used to measure the flow time of DNA in phosphate buffer (Na_2HPO_4/NaH_2PO_4, pH 7.2) with accuracy of 0.01 second and precision of 0.1 second. DNA samples, approximately 200 base pairs in average length, were prepared by sonicating in order to minimize complexities arising from DNA flexibility. Flow time for buffer alone was measured and was termed as t_0. The detail experimental process is reported elsewhere.[1, 2]

(III) By molecular docking with DNA sequence d(ACCGACGTCGGT)$_2$

The rigid molecular docking study has been performed using HEX 8.0 software to determine the orientation of the Ru(III) complexes binding to DNA. Docking was performed and the most stable configuration was chosen as input for investigation. The coordinates of metal complexes were taken from their optimized structure as a .mol file and were converted to .pdb format using CHIMERA 1.5.1 software. HS-DNA used in the experimental work was too large for current computational resources to dock, therefore, the structure of the DNA of sequence d(ACCGACGTCGGT)$_2$ (PDB id: 423D, a familiar sequence used in oligodeoxynucleotide study) obtained from the Protein Data Bank (www.rcsb.org/pdb). All calculations were carried out on an Intel CORE i5, 2.5 GHz based machine running MS Windows 8 64bit as the operating system. The by default parameters were used for the docking calculation with correlation type shape only, FFT mode at 3D level, grid dimension of 6 with receptor range 180 and ligand range 180 with twist range 360 and distance range 40.[5]

(IV) By agarose gel electrophoresis: photo quantization technique

Gel electrophoresis of pUC19 DNA was carried out in TAE buffer (0.04 mol L^{-1} Tris–Acetate, pH 8, 0.001 mol L^{-1} edta). The 15 µL reaction mixture containing 300 mg/L

plasmid DNA in TE buffer (10 mmol L^{-1} Tris, 1 mmol L^{-1} edta, pH 8.0) and 200 µmol L^{-1} complex solution. Reactions were allowed to proceed for 3 h at 37 °C in dark and reactions were satiated by addition of 5 µL loading buffer (0.25% bromophenol blue, 40% sucrose, 0.25% xylene cyanol and 200 m mol L^{-1} edta). The aliquots were loaded directly on to 1% agarose gel and electrophoresed at 50 V in 1× TAE buffer. Gel was stained with 0.5 mg/L ethidium bromide and was photographed on a UV illuminator. The percentage of each form of DNA was capacities. After electrophoresis, the proportion of DNA in each fraction was estimated quantitatively from the intensity of the bands using AlphaDigiDoc™ RT. Version V.4.0.0 PC–Image software. The degree of DNA cleavage activity was expressed in terms of the percentage of conversion of the SC-DNA to OC-DNA and L-DNA according to published literatures.[1, 2, 6]

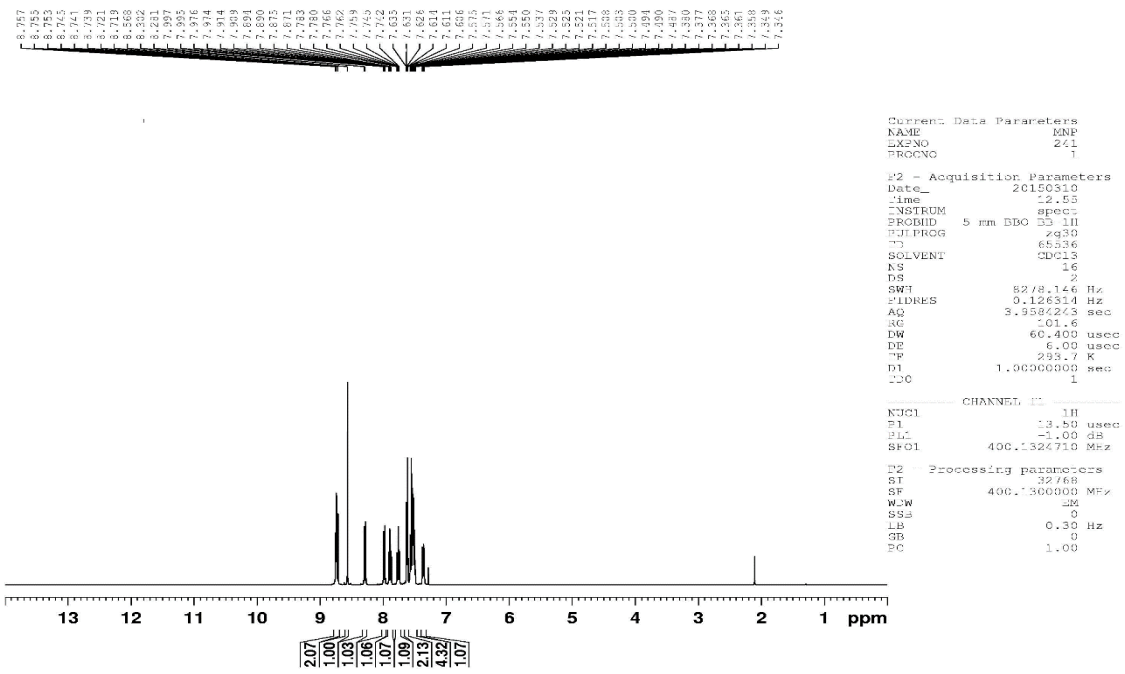
3.5 *In vitro* antimalarial study

All the synthesized compounds were screened for their antimalarial activity against the *Plasmodium falciparum* strain. The *P. falciparum* strain was acquired from Shree R. B Shah Mahavir Superspeciality hospital, Surat, Gujarat, India, and was used in *in vitro* tests. The *P. falciparum* strains were cultivated by a modified method described by Trager and Jensen.[7] The detail experimental process is reported in published articles.[1, 2]

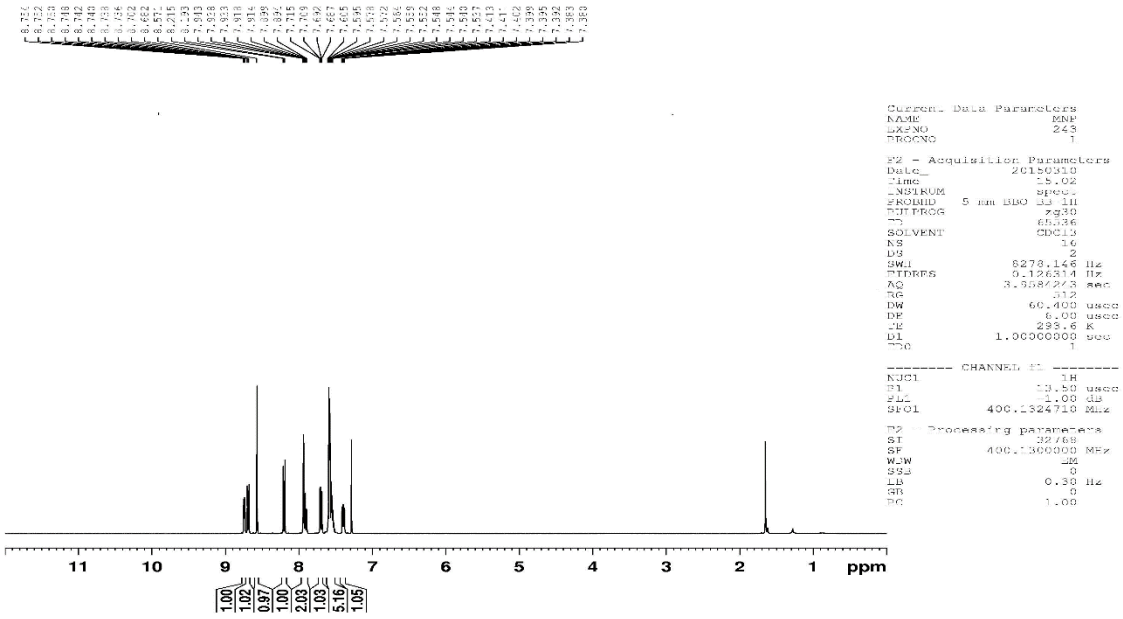
1. J. V. Mehta, S. B. Gajera, D. D. Patel and M. N. Patel, *Applied Organometallic Chemistry*, 2015, **29**, 357-367.
2. J. V. Mehta, S. B. Gajera and M. N. Patel, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 2015, **136, Part C**, 1881-1892.
3. D. Sinha, A. K. Tiwari, S. Singh, G. Shukla, P. Mishra, H. Chandra and A. K. Mishra, *European Journal of Medicinal Chemistry*, 2008, **43**, 160-165.
4. W. Zhong, J.-S. Yu and Y. Liang, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 2003, **59**, 1281-1288.
5. M.-L. Liu, M. Jiang, K. Zheng, Y.-T. Li, Z.-Y. Wu and C.-W. Yan, *Journal of Coordination Chemistry*, 2014, **67**, 630-648.
6. J. Yang, R. N. S. Wong and M. S. Yang, *Chemico-Biological Interactions*, 2000, **125**, 221-232.
7. W. Trager and J. Jensen, *Science*, 1976, **193**, 673-675.

Supplementary material 2: ^{1}H NMR spectra of ligands (3a–3g)

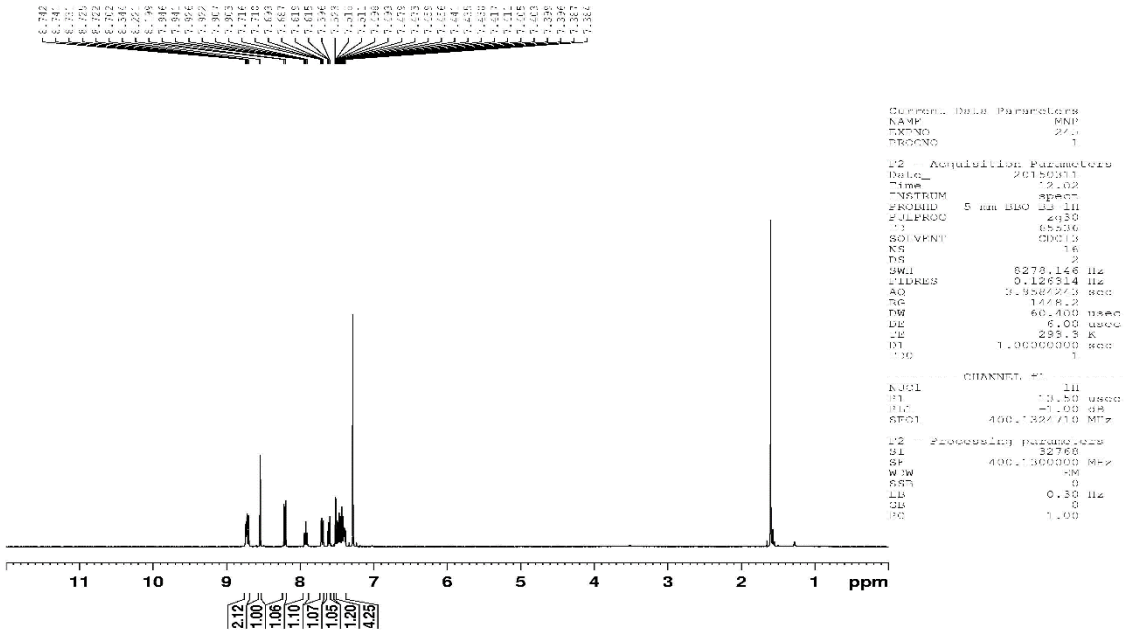
1. 4-phenyl-2-(pyridin-2-yl) quinoline **(3a)**



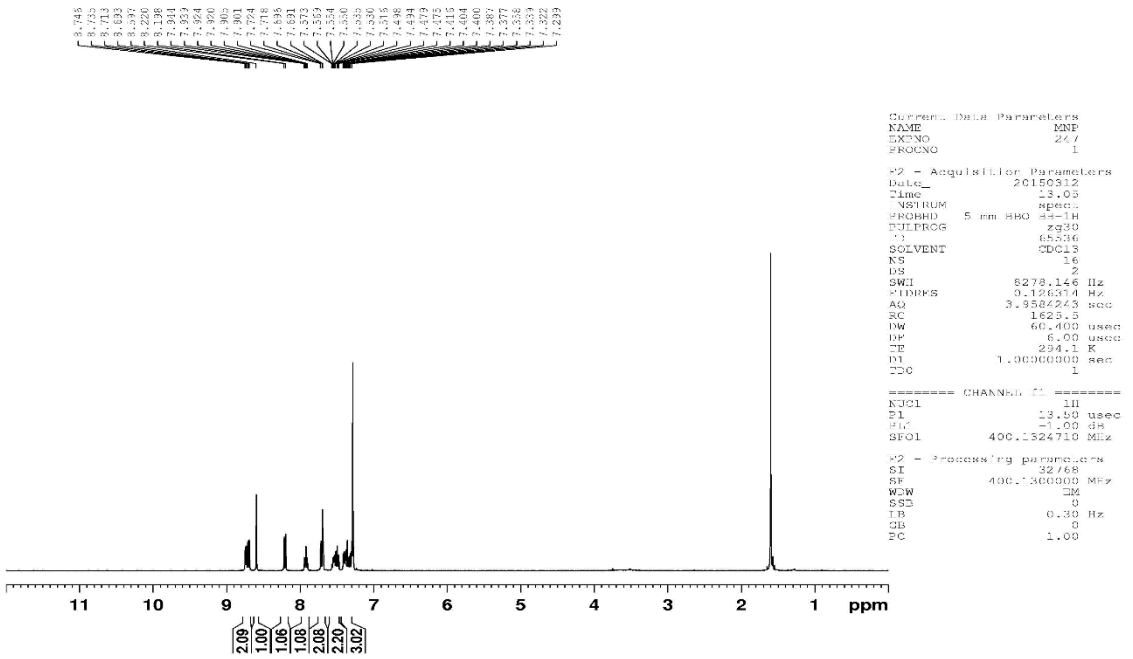
2. 6-chloro-4-phenyl-2-(pyridin-2-yl) quinoline **(3b)**



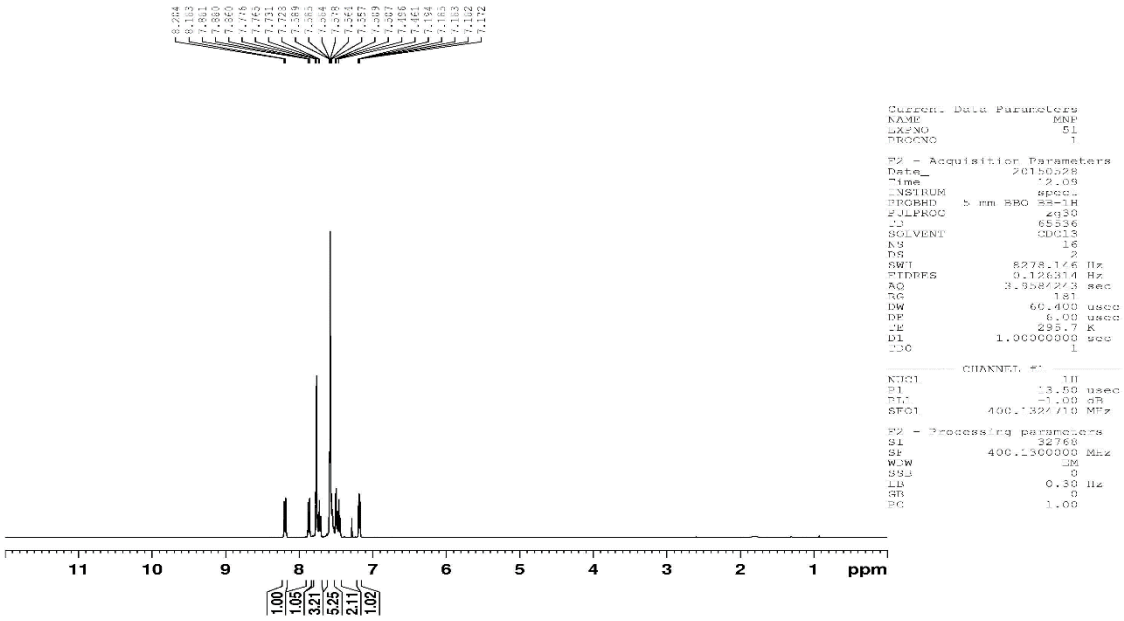
3. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-2-yl) quinoline **(3c)**



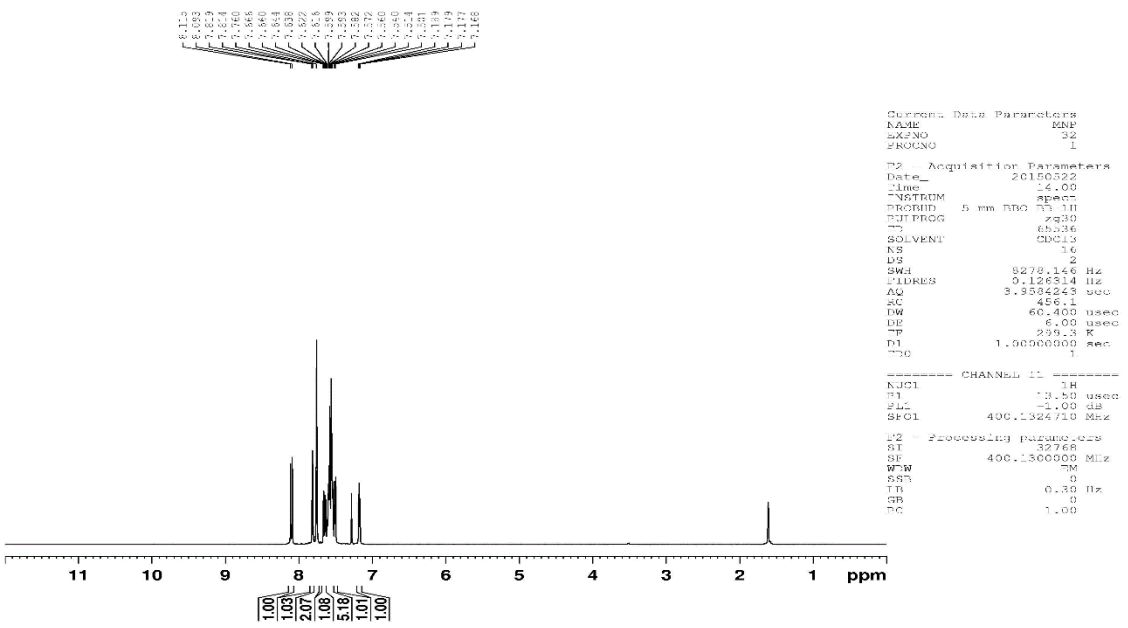
4. 6-chloro-4-(2-fluorophenyl)-2-(pyridin-2-yl) quinoline **(3d)**



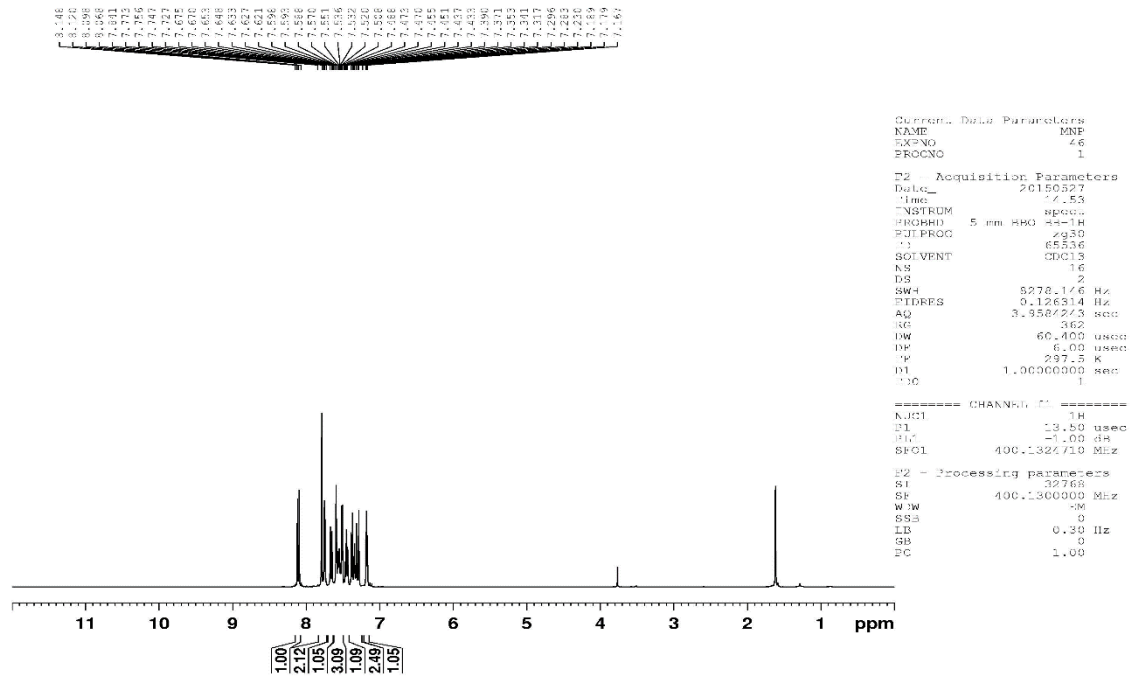
5. 4-phenyl-2-(thiophen-2-yl) quinoline **(3e)**



6. 6-chloro-4-phenyl-2-(thiophen-2-yl) quinoline **(3f)**

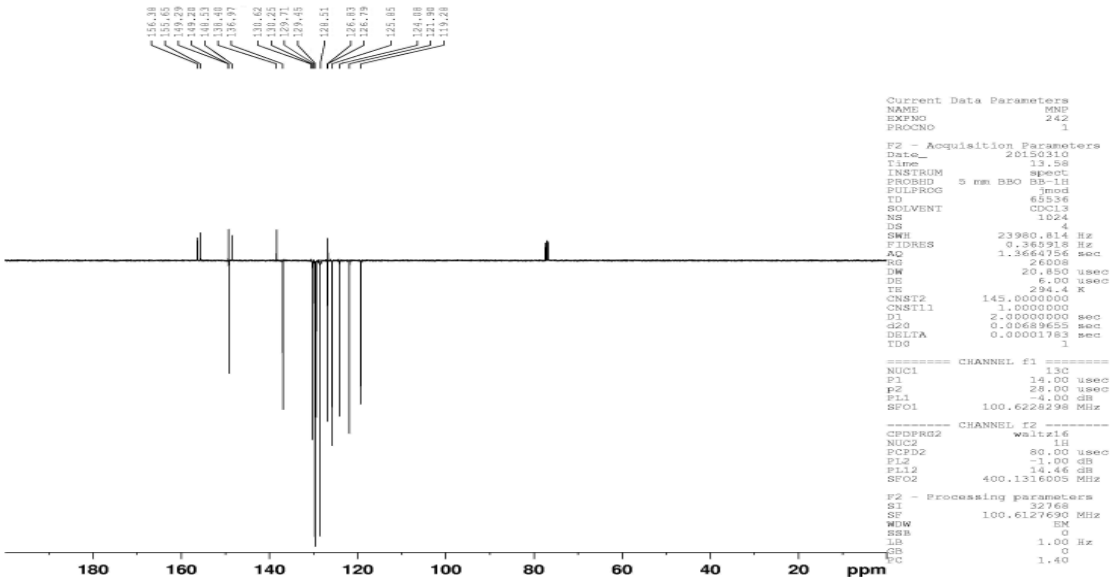


7. 6-chloro-4-(2-fluorophenyl)-2-(thiophen-2-yl) quinoline **(3g)**

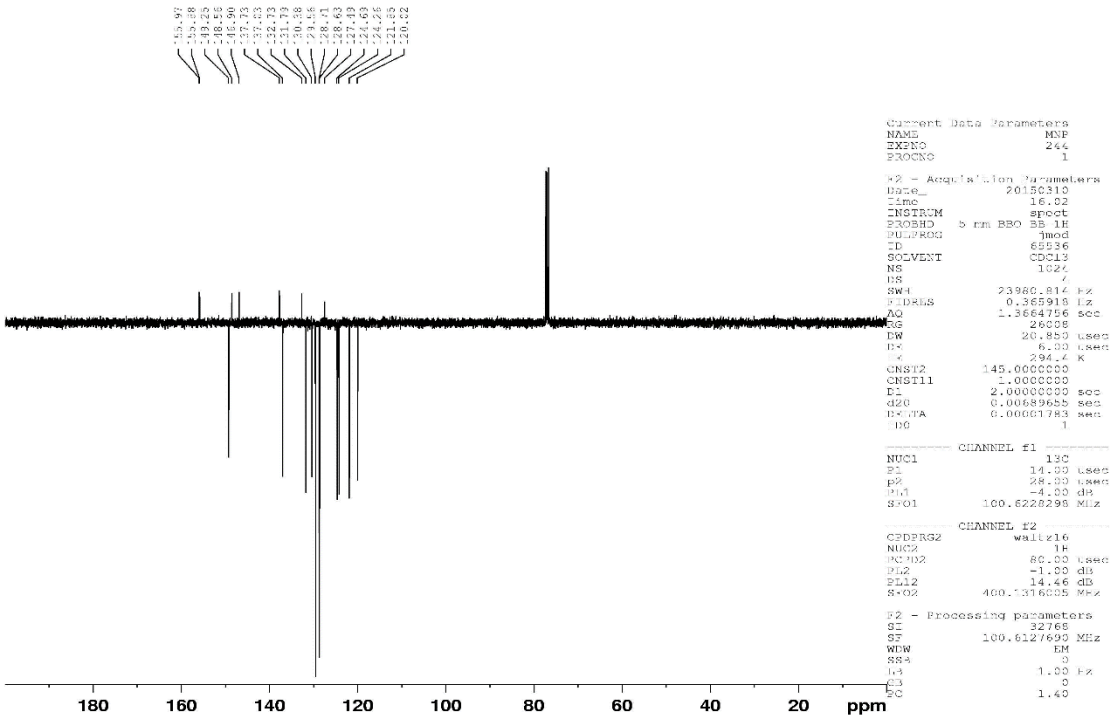


Supplementary material 3: ^{13}C NMR spectra of ligands (3a–3g)

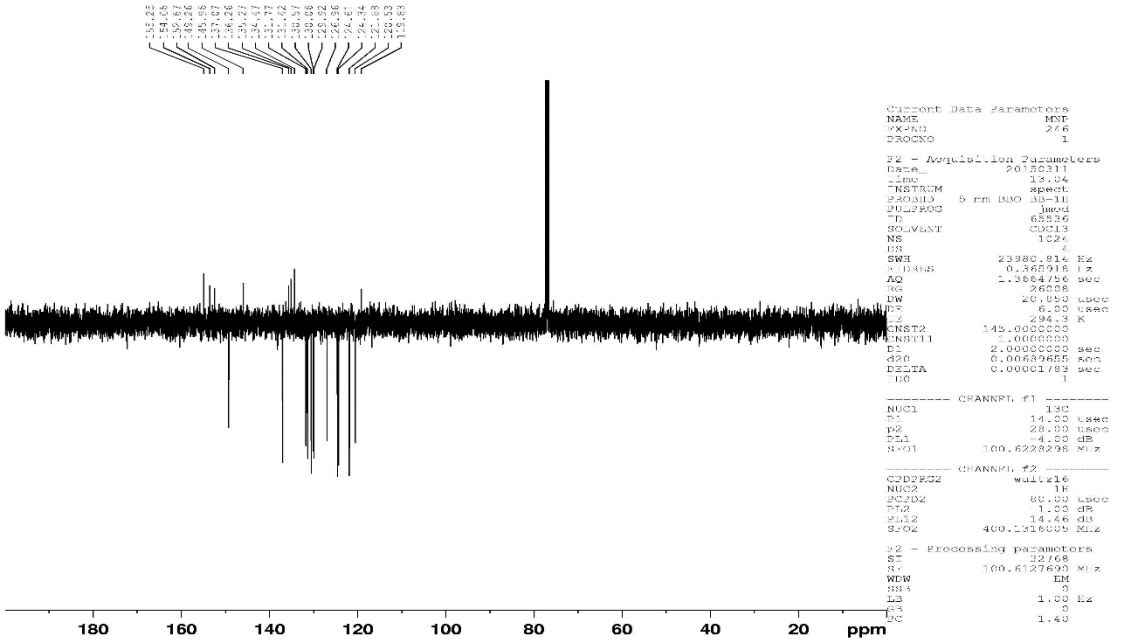
1. 4-phenyl-2-(pyridin-2-yl) quinoline **(3a)**



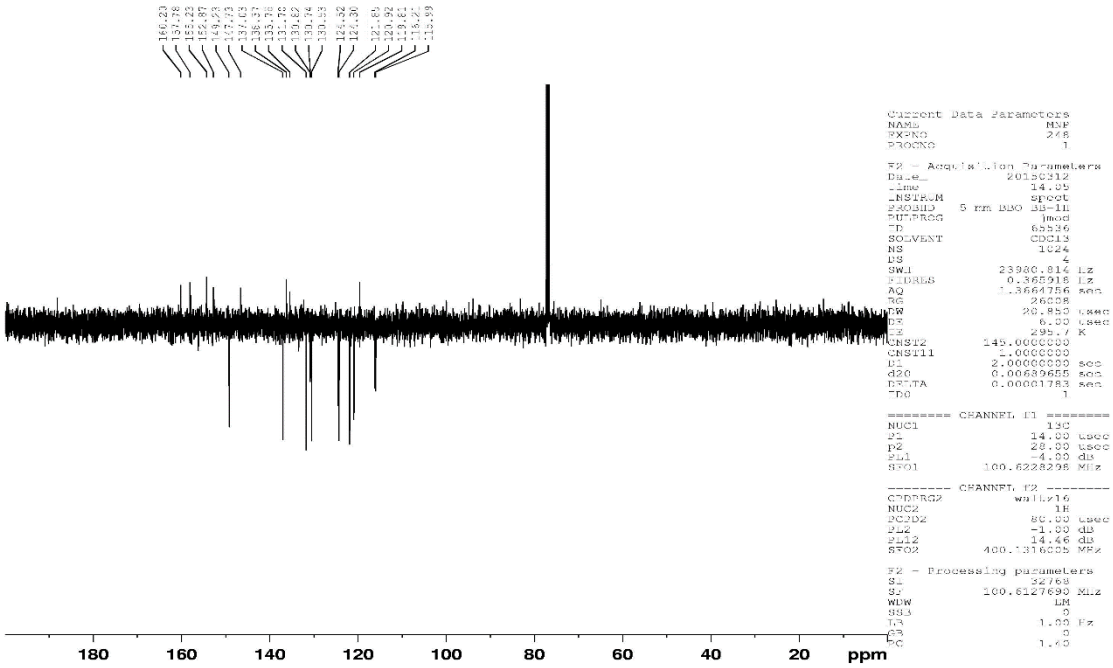
2. 6-chloro-4-phenyl-2-(pyridin-2-yl) quinoline **(3b)**



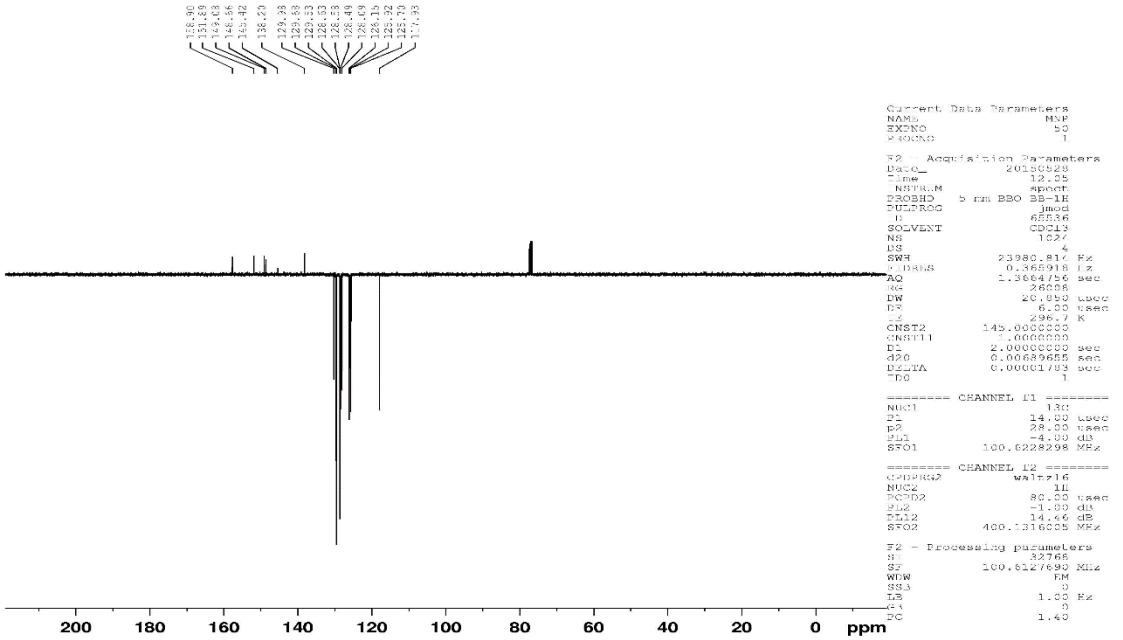
3. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-2-yl) quinoline **(3c)**



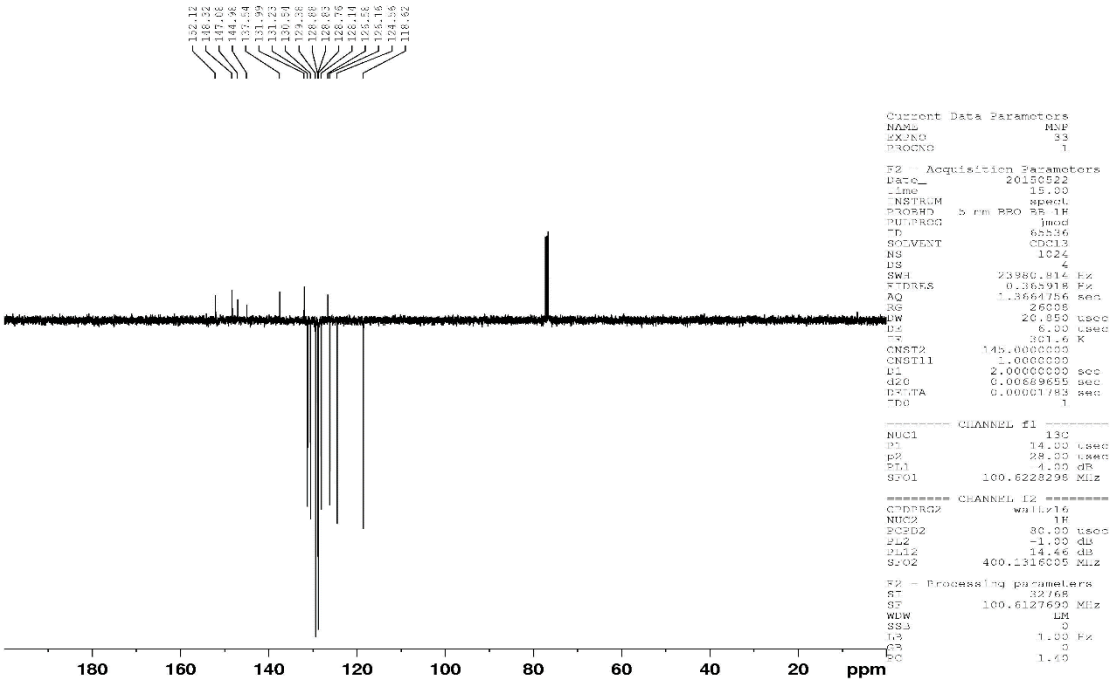
4. 6-chloro-4-(2-fluorophenyl)-2-(pyridin-2-yl) quinoline **(3d)**



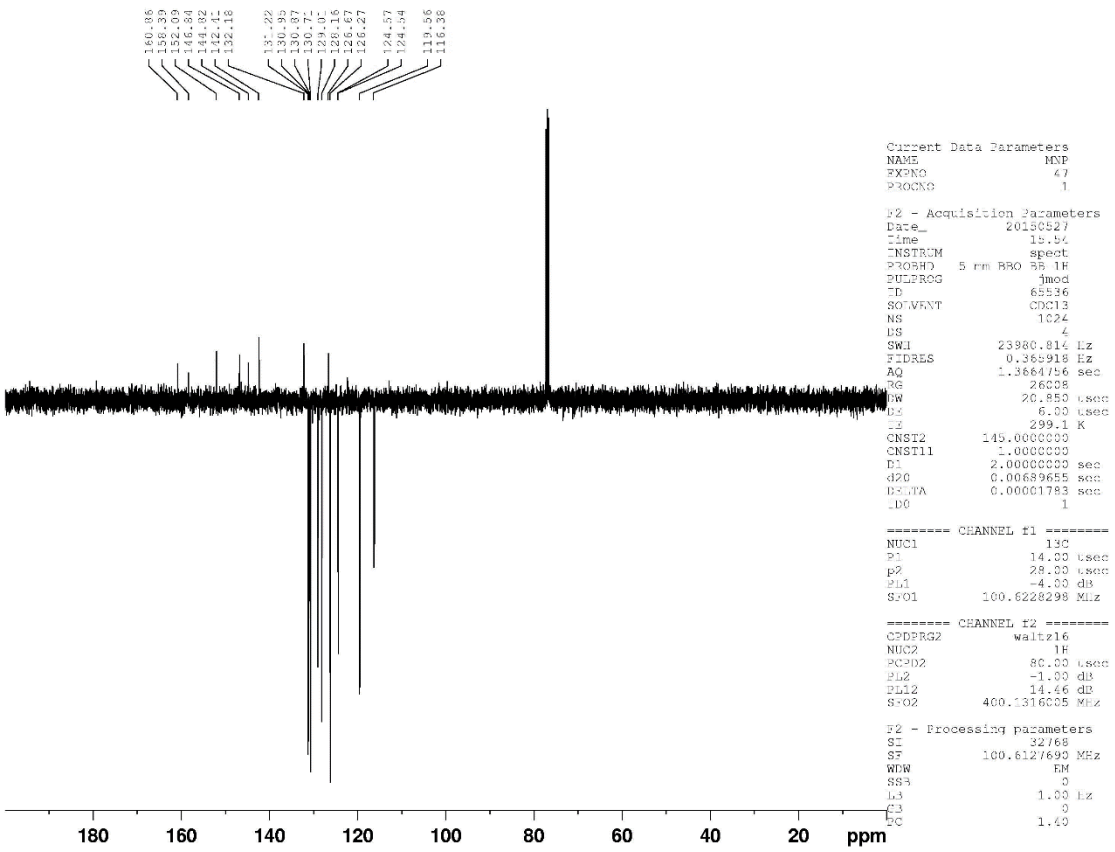
5. 4-phenyl-2-(thiophen-2-yl) quinoline **(3e)**



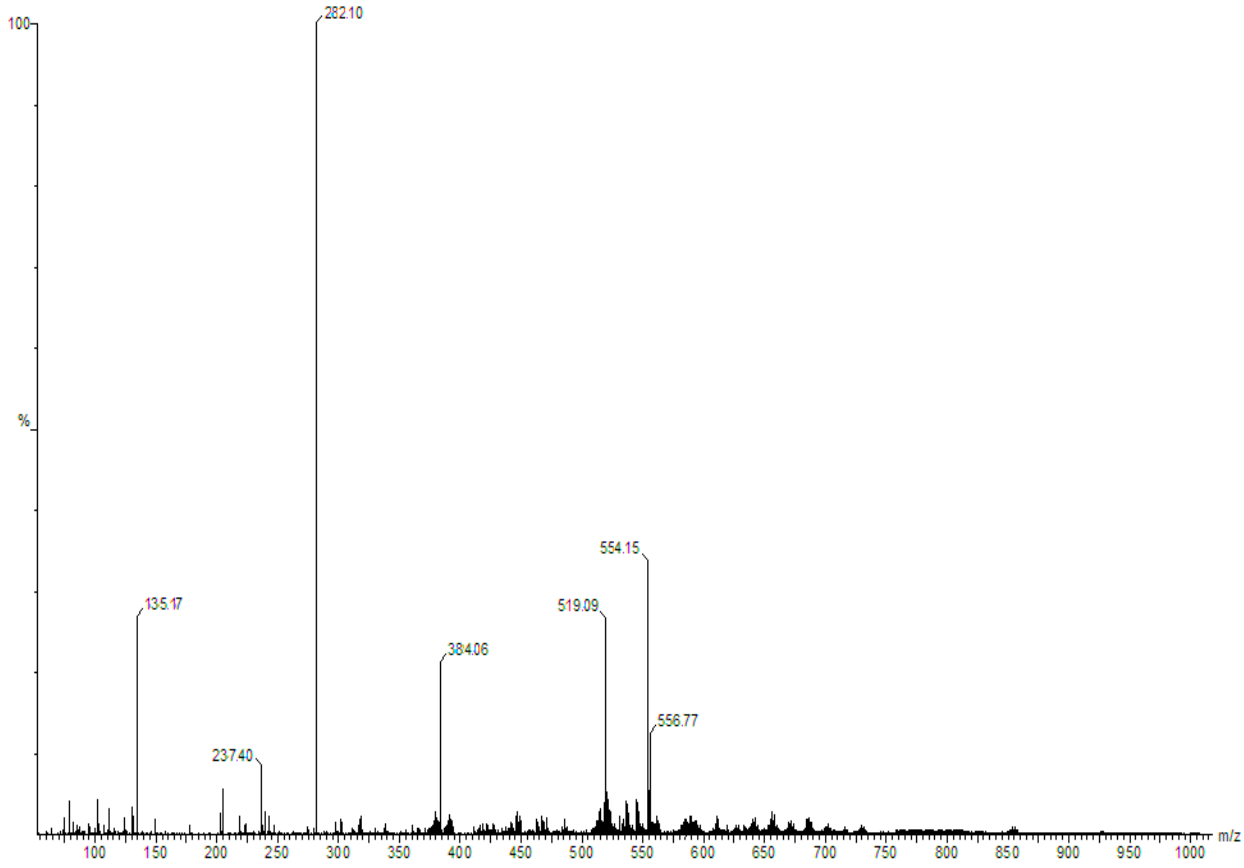
6. 6-chloro-4-phenyl-2-(thiophen-2-yl) quinoline **(3f)**



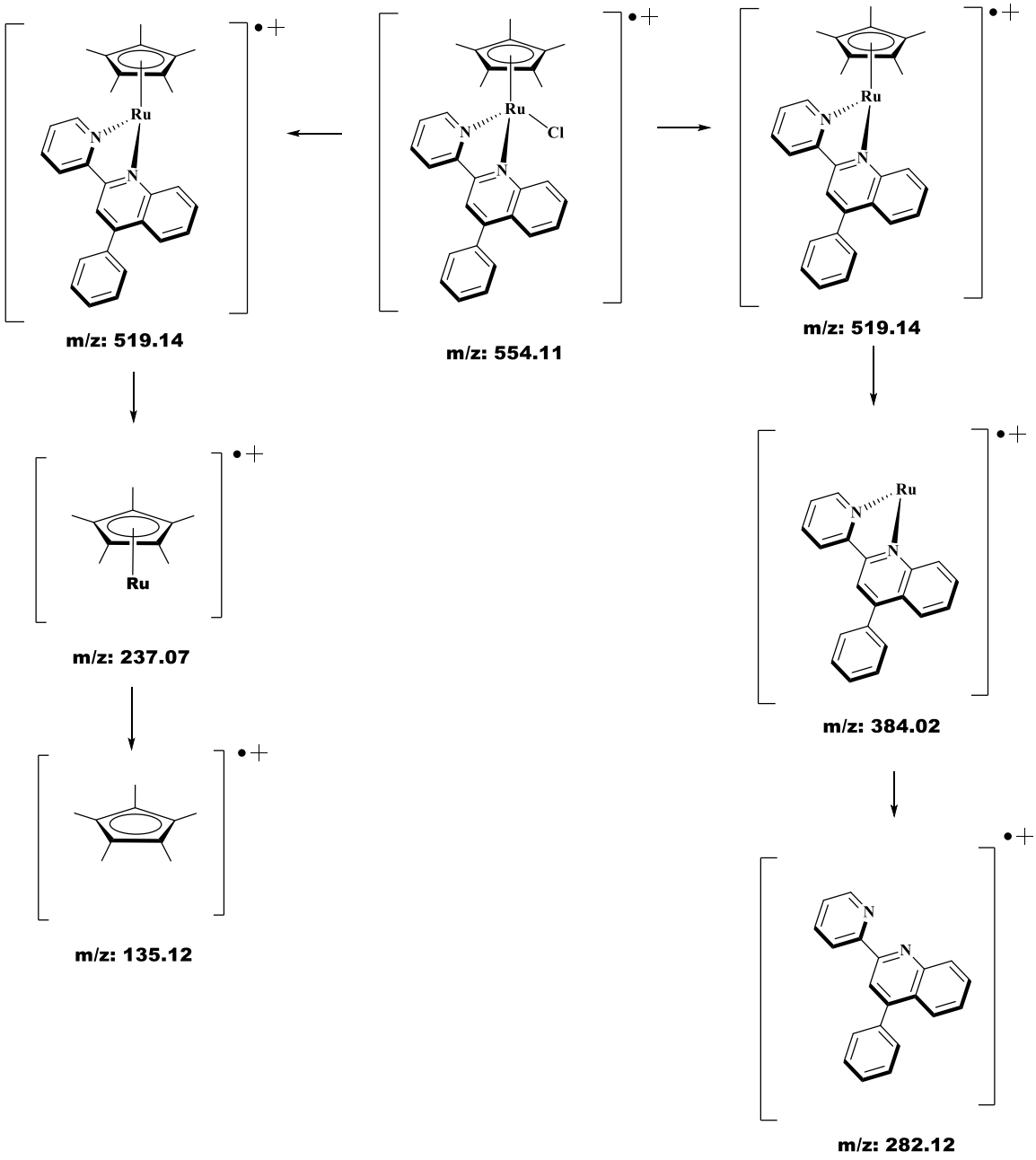
7. 6-chloro-4-(2-fluorophenyl)-2-(thiophen-2-yl) quinoline **(3g)**



Supplementary material 4: LC-mass spectrum of complex **(5a)**



Supplementary material 5: Mass fragmentation pattern of complex **(5a)**



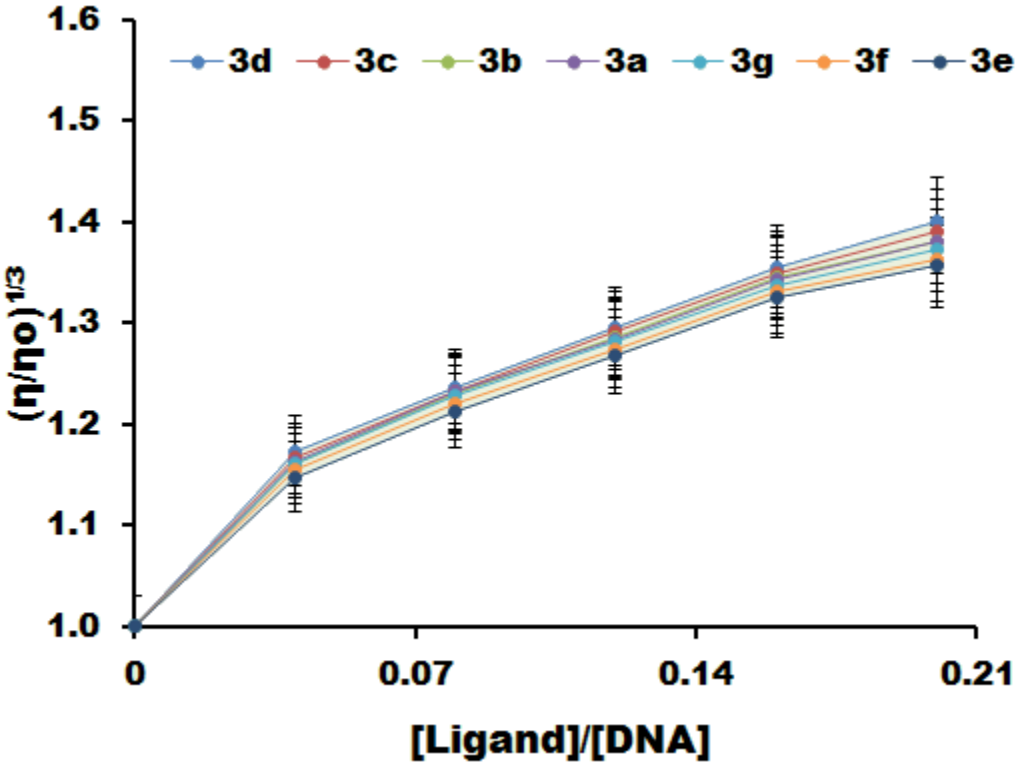
Supplementary material 6: Binding constant (K_b), percentage hypochromicity (%H), bathochromicity ($\Delta\lambda$), IC_{50} (antimalarial) and LC_{50} (*in vitro* cytotoxicity) values of free ligands and synthesized complexes with error uncertainty in the value ±5 %

Compounds	K_b (L mol^{-1})	%H	$\Delta\lambda$ nm	IC_{50}(mg/L)	LC_{50}(mg/L)
3a	0.667±0.01 × 10^5	17.91±0.46	2.6±0.07	1.72±0.03	82.03±2.15
3b	0.701±0.01 × 10^5	17.88±0.48	2.7±0.08	1.70±0.03	77.98±2.03
3c	0.758±0.02 × 10^5	19.06±0.51	2.8±0.08	1.67±0.03	71.74±2.07
3d	0.926±0.02 × 10^5	21.31±0.55	2.7±0.09	1.64±0.02	71.61±1.95
3e	0.349±0.01 × 10^5	19.64±0.55	2.9±0.10	1.84±0.03	119.67±3.55
3f	0.446±0.01 × 10^5	17.76±0.45	2.5±0.07	1.80±0.03	100.90±3.25
3g	0.603±0.01 × 10^5	20.59±0.58	2.8±0.08	1.78±0.03	95.06±3.05
5a	4.05±0.11 × 10^5	20.71±0.52	2.7±0.07	0.63±0.01	8.95±0.22
5b	4.35±0.12 × 10^5	20.23±0.53	2.8±0.08	0.60±0.01	7.99±0.18
5c	4.93±0.13 × 10^5	21.92±0.57	2.6±0.06	0.57±0.01	6.71±0.16
5d	6.25±0.17 × 10^5	23.14±0.78	2.7±0.07	0.55±0.01	5.64±0.17
5e	2.83±0.08 × 10^5	22.48±0.61	2.9±0.10	0.85±0.01	11.45±0.28
5f	2.96±0.09 × 10^5	22.57±0.63	2.7±0.07	0.78±0.01	9.23±0.23
5g	3.37±0.10 × 10^5	20.23±0.61	2.6±0.07	0.72±0.01	9.09±0.22

Supplementary material 7: Bacteriostatic concentration of ligands and synthesized complexes by broth dilution method in terms of MIC in µmol L^{-1} with error uncertainty in the value ±5 %

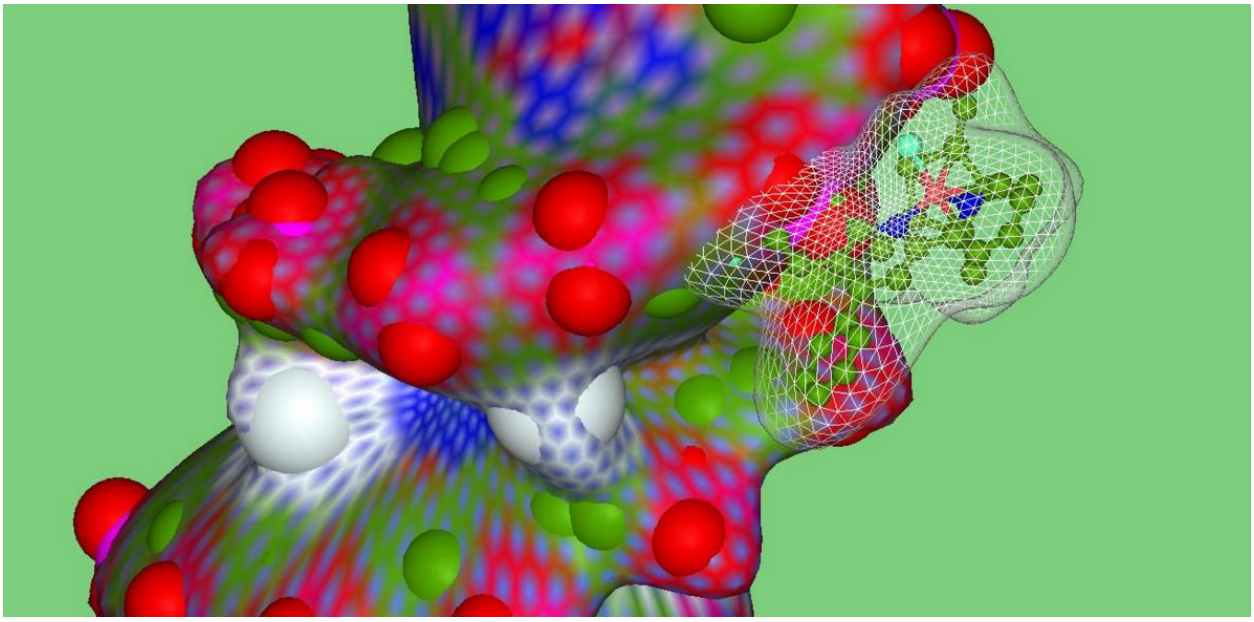
Compounds	Gram(+ve)		Gram(-ve)		
	S. Aureus	*B. subtilis*	*S. marcescens*	*P. aeruginosa*	*E. coli*
3a	279±2	278±3	284±2	280±2	288±2
3b	276±2	273±2	279±2	276±2	281±2
3c	269±2	266±2	272±2	274±2	278±2
3d	260±3	263±2	270±2	268±2	274±2
3e	307±3	316±2	312±2	322±2	317±3
3f	292±3	286±3	293±2	296±3	302±3
3g	285±3	281±2	289±3	286±2	293±2
5a	80±1	82±1	78±1	80±1	82±1
5b	78±1	79±1	75±1	76±1	80±1
5c	73±1	76±1	72±1	73±1	78±1
5d	70±1	74±1	73±1	70±1	75±1
5e	87±1	89±1	86±2	87±2	90±1
5f	85±1	86±1	83±1	85±1	88±1
5g	83±1	86±1	82±1	83±1	86±1

Supplementary material 8: Effect on relative viscosity of HS DNA under the influence of increasing amounts of quinoline ligands at 27 (±0.1) °C in phosphate buffer at pH=7.2 with error uncertainty in the value ±5 %

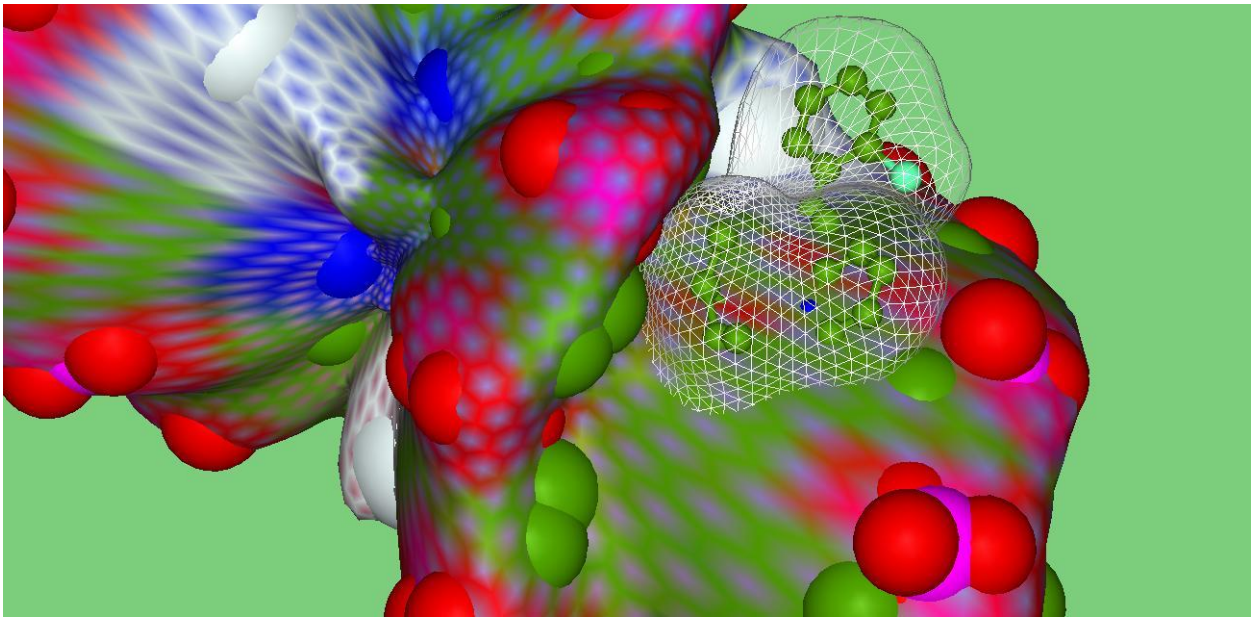


Supplementary material 9: Molecular docking of the complexes 5b–5g and quinoline ligands (3a-3g) (ball and stick) with the DNA duplex (VDW spheres) of sequence d(ACCGACGTCGGT)$_2$. The complex is docked in to the DNA showing intercalation between the DNA base pairs.

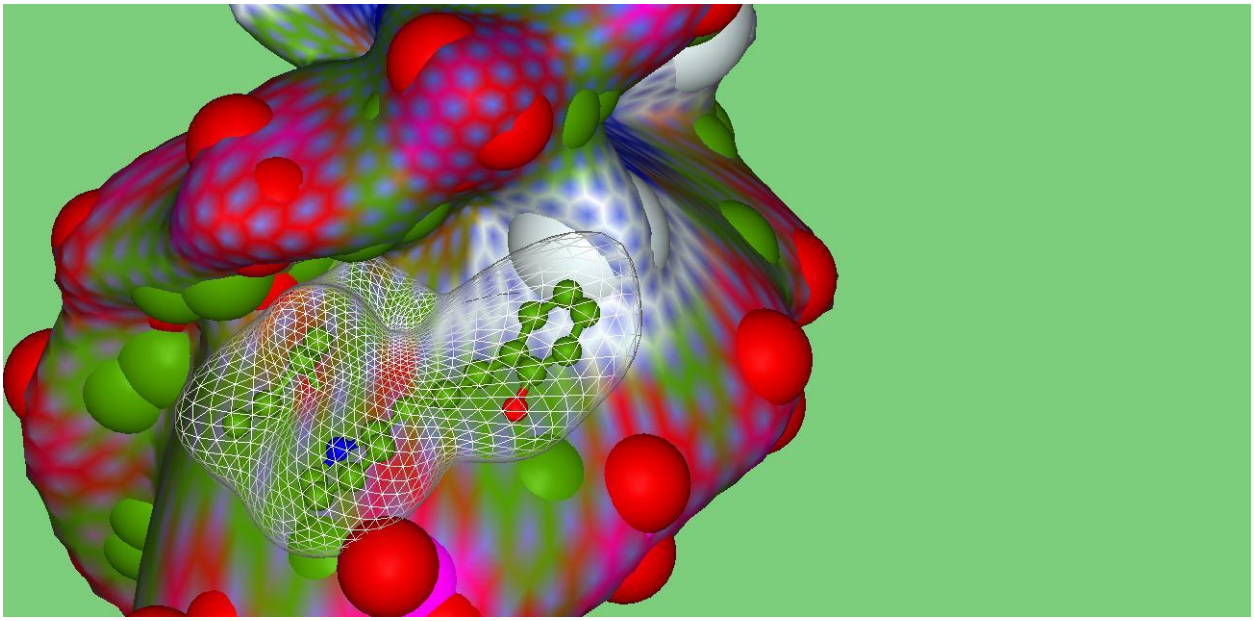
1. Complex **(5b)**



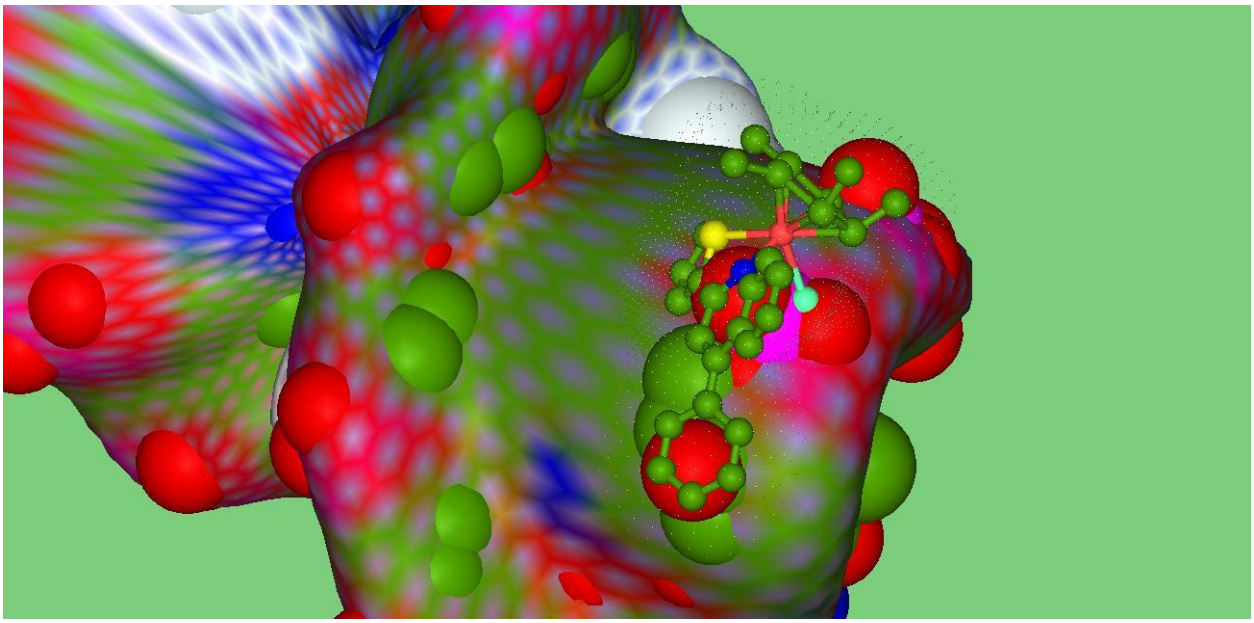
2. Complex **(5c)**



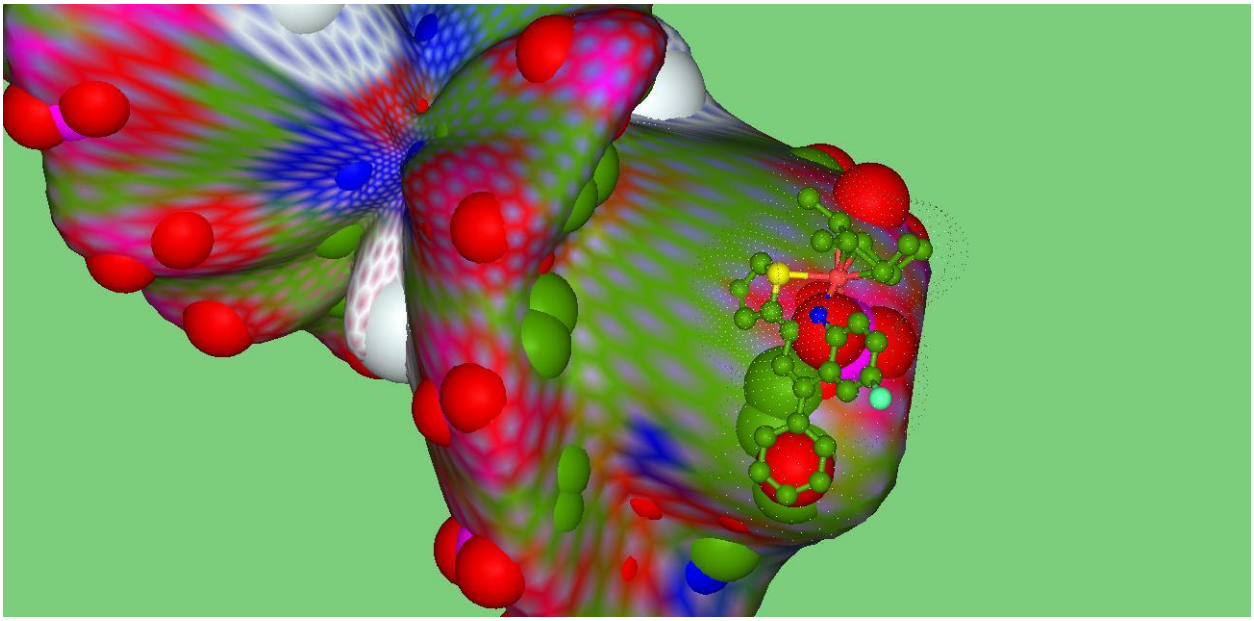
3. Complex **(5d)**



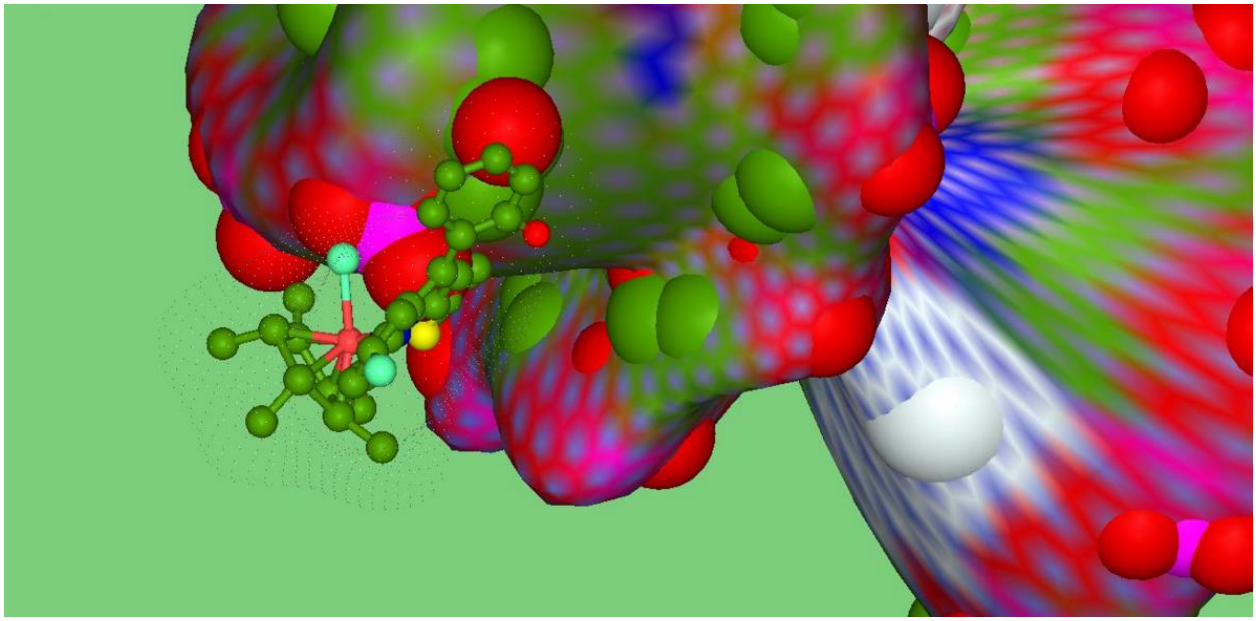
4. Complex **(5e)**



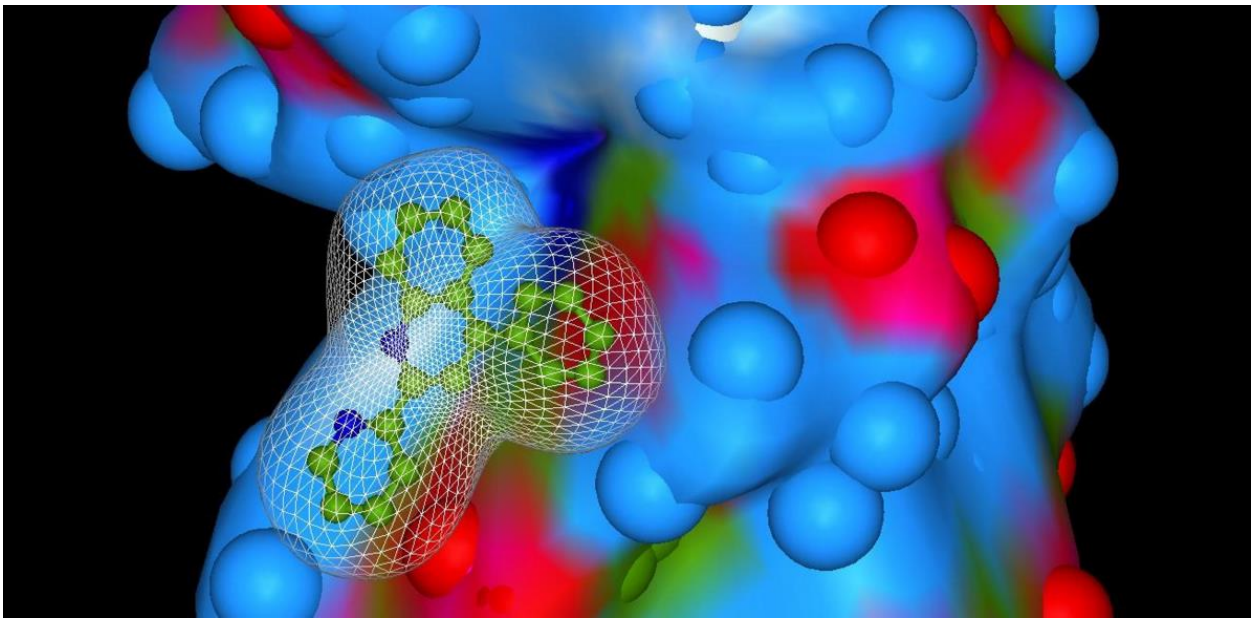
5. Complex **(5f)**



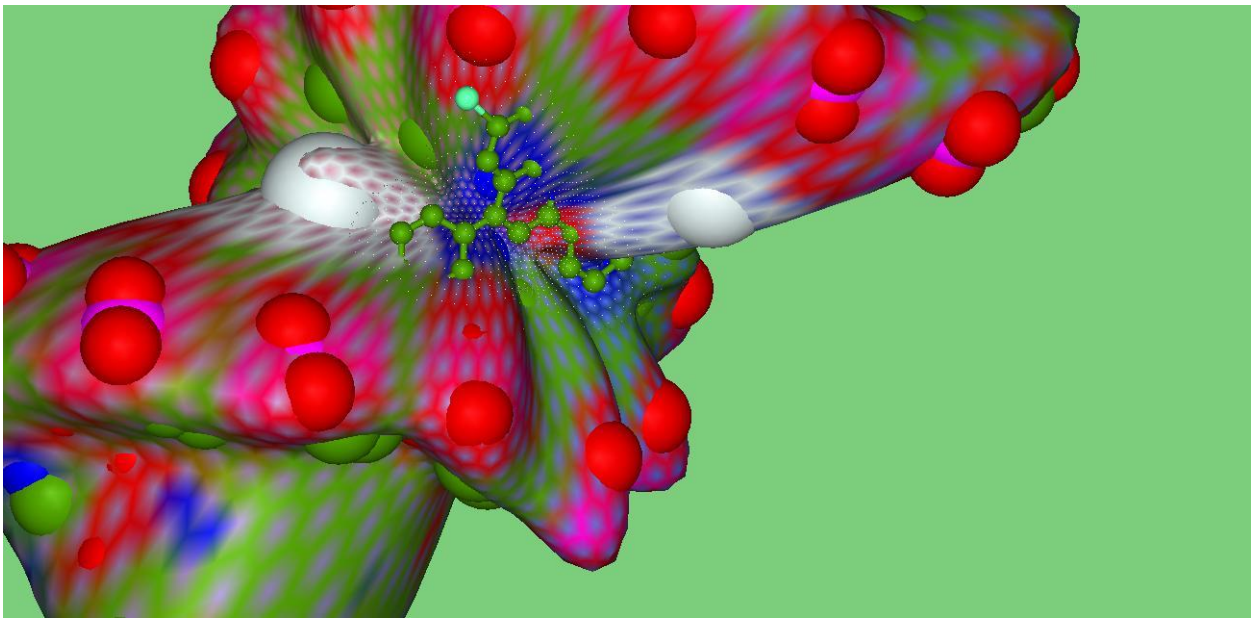
6. Complex **(5g)**



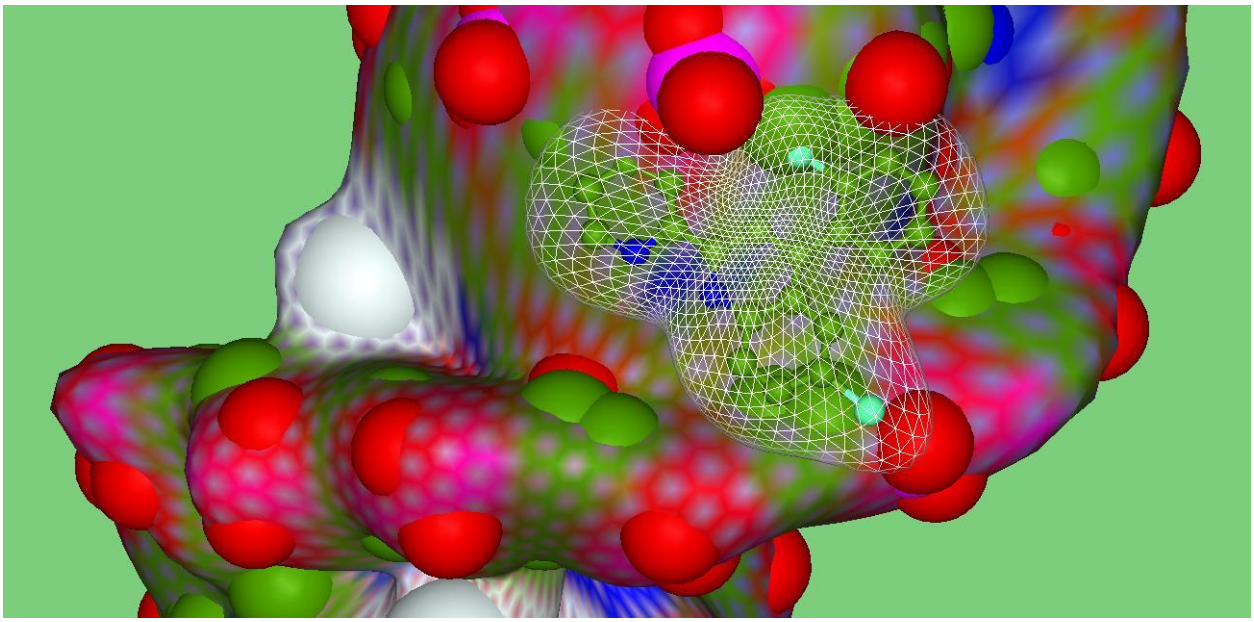
7. 4-phenyl-2-(pyridin-2-yl) quinoline (3a)



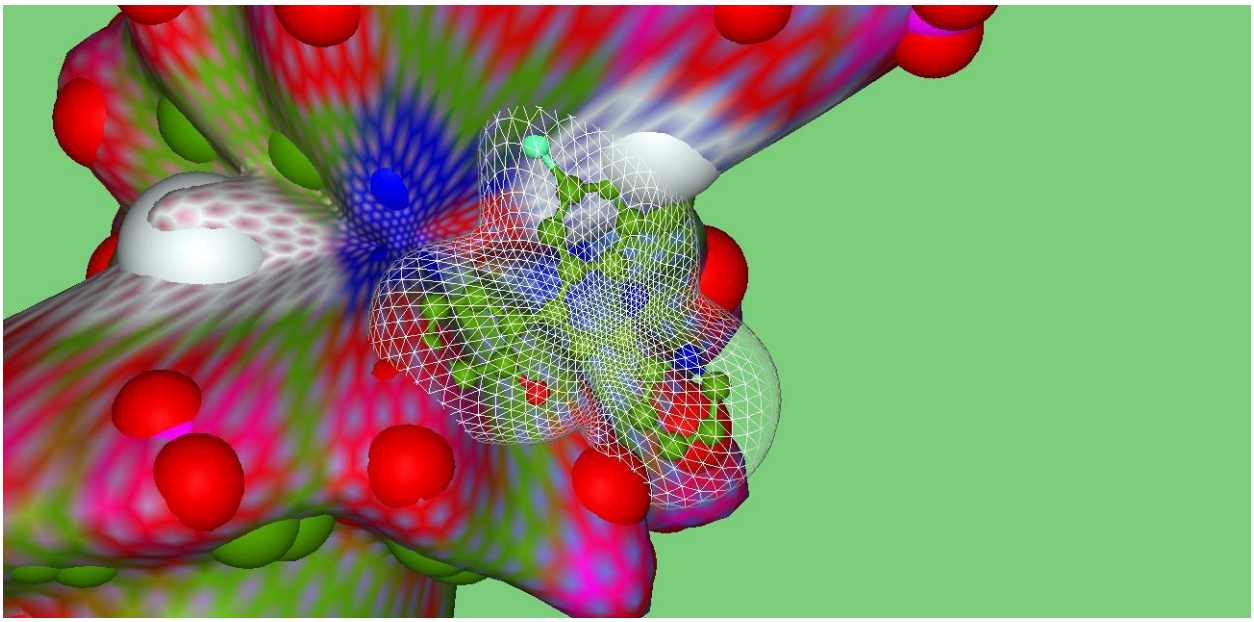
8. 6-chloro-4-phenyl-2-(pyridin-2-yl) quinoline (3b)



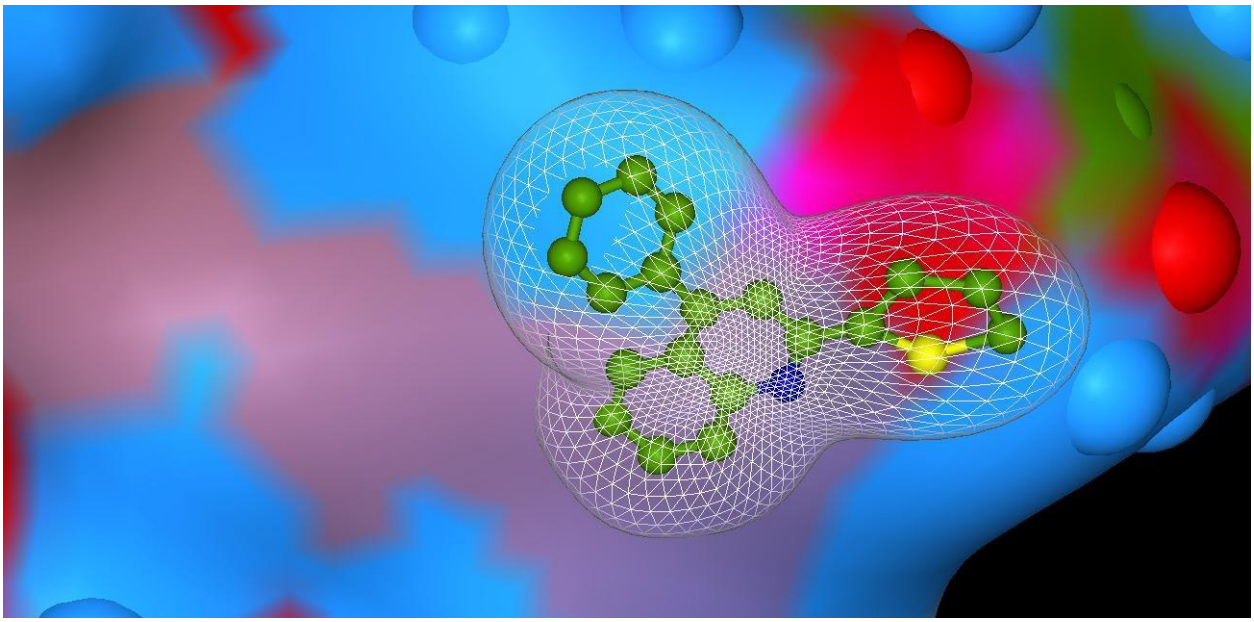
9. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-2-yl) quinoline (3c)



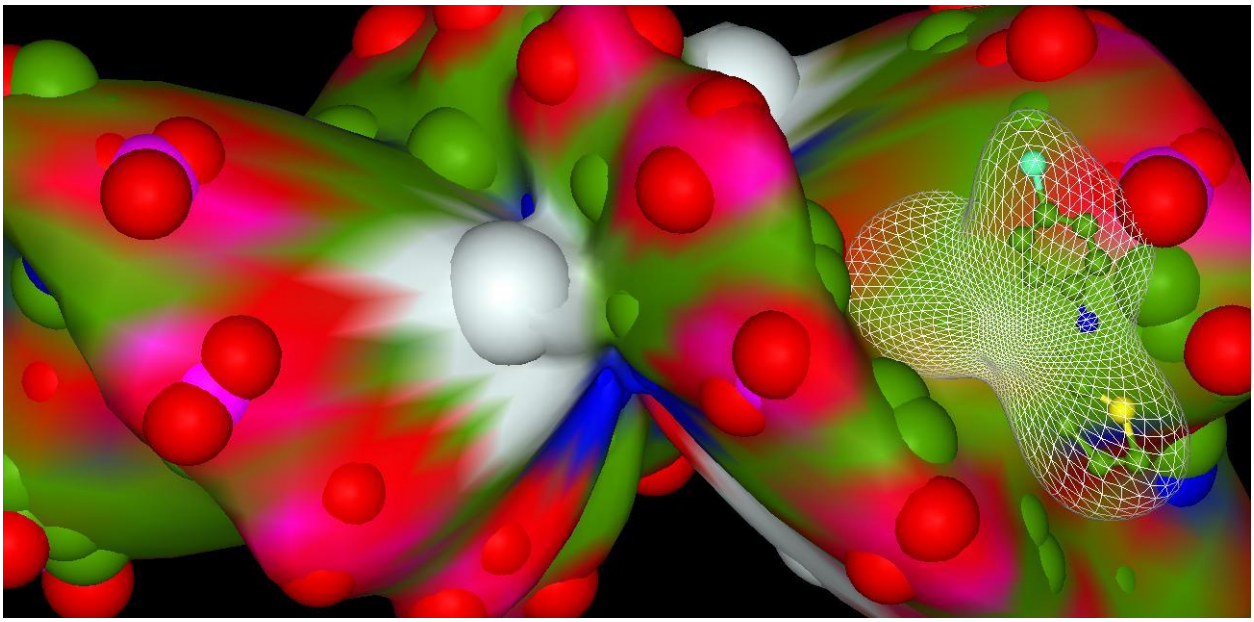
10. 6-chloro-4-(2-fluorophenyl)-2-(pyridin-2-yl) quinoline (3d)



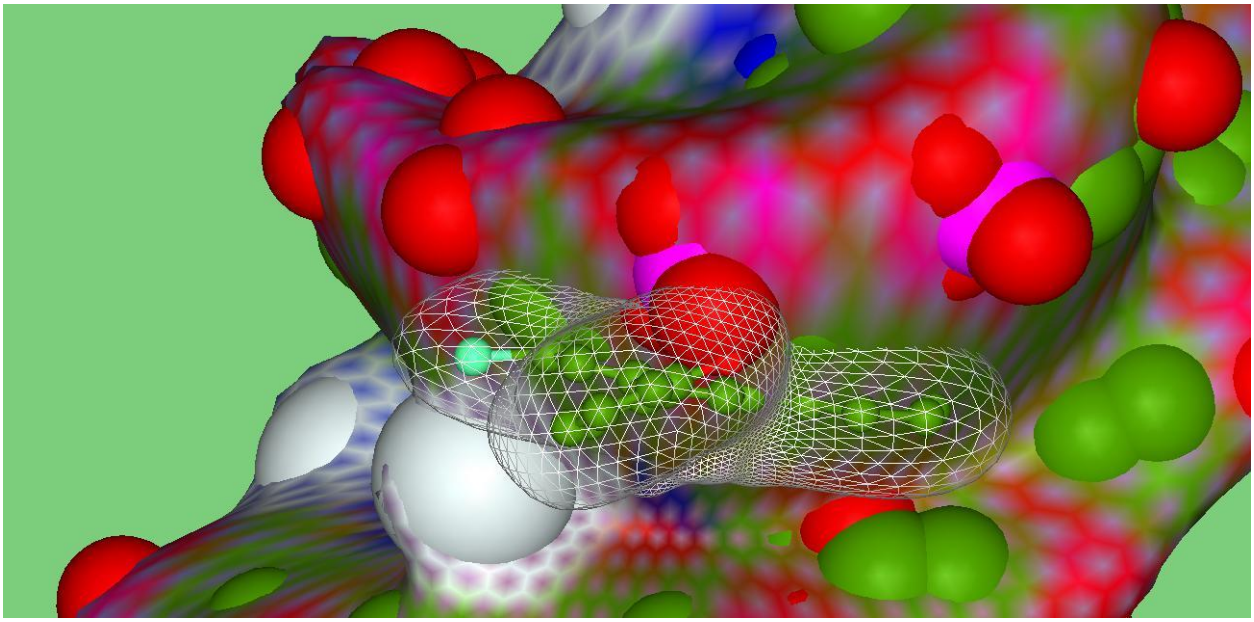
11. 4-phenyl-2-(thiophen-2-yl) quinoline (3e)



12. 6-chloro-4-phenyl-2-(thiophen-2-yl) quinoline (3f)



13. 6-chloro-4-(2-fluorophenyl)-2-(thiophen-2-yl) quinoline (3g)



Supplementary material 10: Compounds mediated DNA cleavage data by agarose gel electrophoresis with error uncertainty in the value ±5 %

Compound	Form I	Form II	Form III	% Cleavage
DNA Control	89±2	11±1	–	–
$RuCl_3 \cdot 3H_2O$	81±2	19±1	–	8.98±0.1
3a	44±1	43±1	13±1	50.56±1.2
3b	43±1	38±1	19±1	51.68±1.3
3c	37±1	46±1	17±1	58.42±1.5
3d	36±1	49±1	15±1	59.55±1.4
3e	39±1	46±1	15±1	56.17±1.2
3f	38±1	42±1	20±1	57.30±1.3
3g	37±1	38±1	25±1	58.42±1.2
5a	24±1	64±1	12±1	73.03±1.8
5b	22±1	53±1	25±1	75.28±1.6
5c	21±1	63±1	16±1	76.40±1.3
5d	20±1	52±1	28±1	77.52±1.2
5e	28±1	47±1	25±1	68.53±1.0
5f	24±1	53±1	24±1	73.03±1.5
5g	22±1	55±1	23±1	75.28±1.4