Transition metal(II) complexes of halogenated derivatives of (*E*)-4-(2-(pyridin-2-ylmethylene)hydrazinyl)quinazoline: Structure, antioxidant activity, DNA-binding DNA-photocleavage, interaction with albumin and *in silico* studies

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Supplementary material

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S1 Binding studies with CT DNA

The interaction of the compounds with CT DNA was studied by UV-vis spectroscopy, viscosity measurements and *via* competitive studies with EB by fluorescence emission spectroscopy.

S1.1 Binding study with CT DNA by UV-vis spectroscopy

The interaction of the compounds with CT DNA has been studied by UV-vis spectroscopy in order to investigate the possible binding modes to CT DNA and to calculate the DNA-binding constants (K_b). The K_b constants (in M^{-1}) were determined by the Wolfe-Shimer equation (eq. S1) [S1] and the plots [DNA]/(ε_A-ε_f) *versus* [DNA] using the UV-vis spectra of the compounds (20-100 μM) recorded for a constant concentration with increasing concentrations of CT DNA for diverse [complex]/[DNA] mixing ratios (= *r*). Control experiments with DMSO were performed and no changes in the spectra of CT DNA were observed. According to the Wolfe-Shimer equation (eq. S1):

$$\frac{[DNA]}{(\varepsilon_A - \varepsilon_f)} = \frac{[DNA]}{(\varepsilon_b - \varepsilon_f)} + \frac{1}{K_b(\varepsilon_b - \varepsilon_f)} \qquad \text{(eq. S1)}$$

where [DNA] is the concentration of DNA in base pairs, $\varepsilon_A = A_{obsd}/[compound]$, ε_f = the extinction coefficient for the free compound and ε_b = the extinction coefficient for the compound in the fully bound form. K_b is given by the ratio of slope to the y intercept in plots [DNA]/(ε_A-ε_f) *versus* [DNA].

S1.2 CT DNA-binding studies by viscosity measurements

The interaction of compounds with DNA has been evaluated *via* the study of the CT DNA viscosity ([DNA] = 0.1 mM) in a buffer solution (150 mM NaCl and 15 mM trisodium citrate at pH 7.0) in the presence of increasing amount of complexes (up to the value of r = 0.36). The obtained data are presented as $(\eta/\eta_0)^{1/3}$ *versus* r, where η is the viscosity of DNA in the presence of the compound, and η_0 is the viscosity of DNA alone in buffer solution.

S1.3 EB-displacement studies

The competition of the complexes with EB was investigated by fluorescence emission spectroscopy in order to examine whether the compounds can displace EB from its DNA-EB conjugate. The CT DNA-EB complex was formed by pre-treating 20 μM EB and 26 μM CT DNA in buffer (150 mM NaCl and 15 mM trisodium citrate at pH 7.0). The possible displacement of EB by the compounds and subsequently their intercalating effect was studied by the stepwise addition of a certain amount of the solution of each compound into the solution of the CT DNA-EB adduct. The solutions were excited at 540 nm and the emission was monitored from 550-700 nm with λ_{max} = 592-595 nm and the effect of the addition of each compound to the CT-DNA EB solution was recorded. The compounds do not display any fluorescence emission bands at room temperature in solution or in the presence of CT DNA or EB under the same experimental conditions (λ_{ex} = 540 nm); therefore, the observed quenching of the EB-DNA solution may be attributed to the displacement of EB from its EB-DNA adduct.

The Stern-Volmer constants (K_{SV}, in M^{-1}) were calculated according by the linear Stern-Volmer equation (eq. S2) [S2] and the respective plots Io/I *versus* [compound].

$$\frac{Io}{I} = 1 + k_q\tau_0[Q] = 1 + K_{SV}[Q] \qquad \text{(eq. S2)}$$

where Io and I are the emission intensities of the EB-DNA solution in the absence and the presence of the compounds, respectively, τ_o = the average lifetime of the emitting system without the quencher and kq = the quenching constant. Taking τ_o = 23 ns as the fluorescence lifetime of the EB-DNA adduct [S3], the quenching constants (k_q, in $M^{-1}s^{-1}$) of the compounds were calculated according to eq. S3 [S2]:

$$K_{SV} = k_q\tau_o \qquad \text{(eq. S3)}$$

S2 Plasmid DNA photo-cleavage experiments

The reaction mixtures (20 μL) containing supercoiled circular pBR322 plasmid DNA stock solution (Form I, 50 μM/base pair, ~500 ng), compounds, and Tris buffer (25 μM, pH 6.8) in Pyrex vials were incubated for 30 min at 37 °C, centrifuged, and then irradiated with UVB light (312 nm - 18 W for 30 min) or UVA light (365 nm - 18 W for 2 h) or white light (18 W for 2 h) being at 10 and 15 cm distance, respectively, under aerobic conditions at room temperature.

After addition of the gel-loading buffer [6x Orange DNA Loading Dye 10 mM Tris-HCl (pH 7.6), 0.15% orange G, 0.03% xylene cyanol FF, 60% glycerol, and 60 mM EDTA, by Fermentas], the reaction mixtures were loaded on a 1% agarose gel with EB staining. The electrophoresis tank was attached to a power supply at a constant current (75 V for 30 minutes). The gel was visualized by the Mupid-ONE LED Illuminator and photographed by a Nikon Digital Camera D3400. Quantification of DNA−cleaving activities was performed by integration of the optical density as a function of the band area using the program "Image J" available at the site http://rsb.info.nih.gov/ij/download.html.

The ss% and ds% damages were calculated according to the equations S4 and S5:

$$ss\% = \frac{FormII}{(FormI + FormII + FormIII)} \times 100 \qquad \text{(eq. S4)}$$

$$ds\% = \frac{FormIII}{(FormI + FormII + FormIII)} \times 100 \qquad \text{(eq.S5)}$$

where, as Form II we consider Form II of each series minus Form II of the irradiated control DNA and as Form I, we consider Form I of each series. The amount of supercoiled DNA was multiplied by factor of 1.43 to account for reduced EB intercalation into supercoiled DNA [S4].

S3 Antioxidant activity assay

The antioxidant activity of the compounds was evaluated *via* their ability to scavenge *in vitro* free radicals such as DPPH and ABTS and to reduce H_2O_2. All the experiments were carried out at least in triplicate and the standard deviation of absorbance was less than 10% of the mean.

S3.1 Determination of the reducing activity of the radical DPPH

To an ethanolic solution of DPPH (0.1 mM) an equal volume solution of the compounds (0.1 mM) in ethanol was added. Absolute ethanol was also used as control solution. The absorbance at 517 nm was recorded at room temperature after 30 and 60 min, in order to examine the possible existence of a potential time-dependence of the DPPH radical scavenging activity [S5]. The DPPH-scavenging activity of the compounds was expressed as the percentage reduction of the absorbance values of the initial DPPH solution (DPPH%). NDGA and BHT were used as reference compounds.

S3.2 Assay of radical cation ABTS-scavenging activity

The ABTS assay was performed to determine the activity of the compounds to scavenge the radical cation ABTS. Initially, a water solution of ABTS was prepared (2 mM). ABTS radical cation ($ABTS^{+\cdot}$) was produced by the reaction of ABTS stock solution with potassium persulfate (0.17 mM) and the mixture was stored in the dark at room temperature for 12-16 h before its use. The ABTS was oxidized incompletely because the stoichiometric reaction ratio of ABTS and potassium persulfate is 1:0.5. The absorbance became maximal and stable only after more than 6 h of reaction although the oxidation of the ABTS started immediately. The radical was stable in this form for more than 2 days when allowed to stand in the dark at room temperature. Afterwards, the $ABTS^{+\cdot}$ solution was diluted in ethanol to an absorbance of 0.70 at 734 nm and 10 μL of diluted compounds or standards (0.1 mM) in DMSO were added. The absorbance was recorded out exactly 1 min after initial mixing [S5]. The ABTS radical scavenging activity was expressed as the percentage inhibition of the absorbance of the initial ABTS solution (ABTS%). Trolox was used as an appropriate standard.

S3.3 Reduction of hydrogen peroxide

The ability of the compounds to reduce hydrogen peroxide (H_2O_2) was estimated according to the method described in the literature [S6]. The reaction mixture contained 20 μL of each of the tested compounds (0.1 mM) and 5 μL H_2O_2 solution (40 mM) in phosphate buffer (50 mM, pH 7.4). The absorbance was measured at 230 nm after 10 min. The antioxidant activity (reduction of hydrogen peroxide) of the compounds was expressed as the percentage decrease of the initial H_2O_2 solution (H_2O_2%). L-ascorbic acid (or vitamin C) was used as a standard.

S4 Albumin assays

S4.1 Albumin-binding studies

In order to investigate if the compounds can bind to carrier protein like serum albumins, we carried out albumin binding study by tryptophan fluorescence quenching experiments using bovine serum albumin (BSA, 3 μM) in buffer (containing 15 mM trisodium citrate and 150 mM NaCl at pH 7.0). The quenching of the emission intensity of tryptophan residues of BSA at 343 nm was monitored using the compounds as quenchers with increasing concentration [S2]. The fluorescence emission spectra of the compounds were also recorded with λ_{ex} = 295 nm. No fluorescence emission band was recorded and thus it was not related to the compounds. The influence of the inner-filter effect [S7] on the measurements was evaluated by equation S6.

$$I_{corr} = I_{meas} \times 10^{\frac{\varepsilon(\lambda_{exc})cd}{2}} \times 10^{\frac{\varepsilon(\lambda_{em})cd}{2}} \quad \text{(eq. S6)}$$

where I_{corr} = corrected intensity, I_{meas} = the measured intensity, c = the concentration of the quencher, d = the cuvette (1 cm), $\varepsilon_{(\lambda exc)}$ and $\varepsilon_{(\lambda em)}$ = the ε of the quencher at the excitation and the emission wavelength, respectively, as calculated from the UV-vis spectra of the compound [S7].

The Stern-Volmer and Scatchard graphs are used to study the interaction of the compounds with serum albumins. According to Stern-Volmer quenching equation (eq. S2), where Io = the initial tryptophan fluorescence intensity of SA, I = the tryptophan fluorescence intensity of SA after the addition of the quencher, k_q = the quenching constant, K_{SV} = the Stern-Volmer constant, τ_o = the average lifetime of SA without the quencher, and, taking as fluorescence lifetime (τ_o) of tryptophan in SA at around 10^{-8} s [S2] K_{SV} (in M^{-1}) can be obtained by the slope of the diagram Io/I *versus*

[compound] (Stern-Volmer plots), and subsequently the quenching (k_q, in $M^{-1}s^{-1}$) may be calculated from eq. S3.

From the Scatchard equation (eq. S7):

$$\frac{\Delta I / Io}{[Q]} = nK - K\frac{\Delta I}{Io} \qquad \text{(eq. S7)}$$

where n is the number of binding sites per albumin and K is the SA-binding constant (K, in M^{-1}) is calculated from the slope in plots (ΔI/Io)/[complex] *versus* ΔI/Io and n is given by the ratio of y intercept to the slope [S8].

S4.2 Competitive SA-fluorescence studies with warfarin and ibuprofen

The competitive studies with warfarin or ibuprofen (site probes) [S9] were performed by tryptophan fluorescence quenching experiments using a fixed concentration of BSA and site probes (3 μM) in buffer (containing 15 mM trisodium citrate and 150 mM NaCl at pH 7.0). The fluorescence emission spectra were recorded in the presence of increasing amounts of the compounds as quenchers with an excitation wavelength of 295 nm. The Scatchard equation (eq. 7) [S2] and plots were applied on the corrected SA-fluorescence emission spectra in order to determine the BSA-binding constant of the compounds in the presence of warfarin or ibuprofen.

S5. *In silico* computational methods: (molecular modeling and docking calculations)

Complexes **1-6** were built in 3D coordinates and their best most stable (lowest energy) conformation was detected by geometrical optimization of its structure in the gas phase, as implemented in the Spartan '14 Molecular Modelling program suite [S10]. The structure of the molecule was initially optimized (via energy minimization) by conformational search using the Monte Carlo method with the MMFF94 molecular mechanics model, included in the Spartan '14 program suite. Geometry optimization (leading to the most stable conformer with the lowest energy) was accomplished via quantum-chemical calculations by utilizing the *ab initio* Hartree-Fock method with a 6-31G* basis set. The molecular docking studies were carried out on the crystal structure of BSA and CT DNA (^{101}Gp ^{102}Ap ^{103}Ap ^{104}Tp ^{105}Tp ^{106}Gp ^{107}Tp ^{108}Ap ^{109}Ap ^{110}Gp ^{111}Cp ^{112}Gp ^{113}Cp) (Protein Data Bank, PDB entry code: 2BXG, 6QS9 and 2BJC, respectively). The molecular docking simulations were performed by the open-source program AutoDock Vina [S11]. The produced compound-protein/DNA conjugates were ranked by the energy score, including their binding conformations. Best docked poses, with both lower binding energies and stronger interaction pattern were derived from the docking results. UCSF Chimera was used to visualize the molecules and the results of the docking and to construct the molecular models [S12].

S6 References

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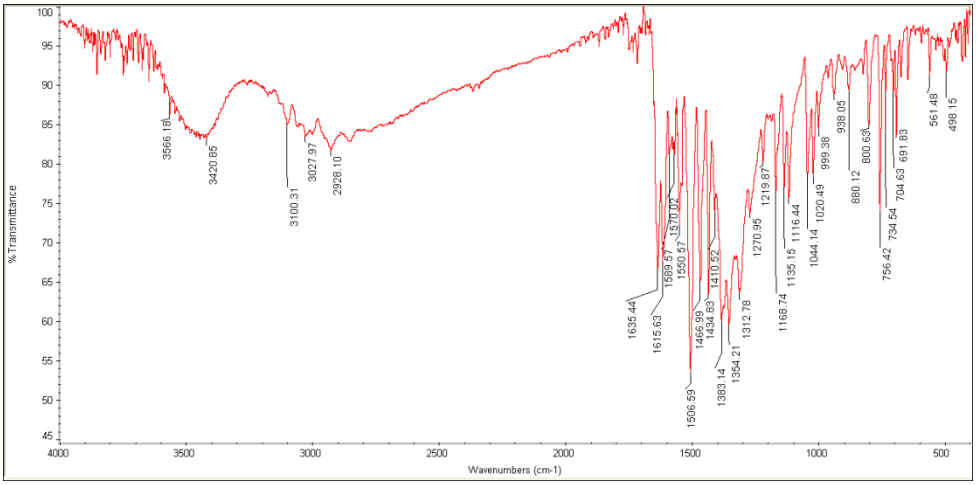
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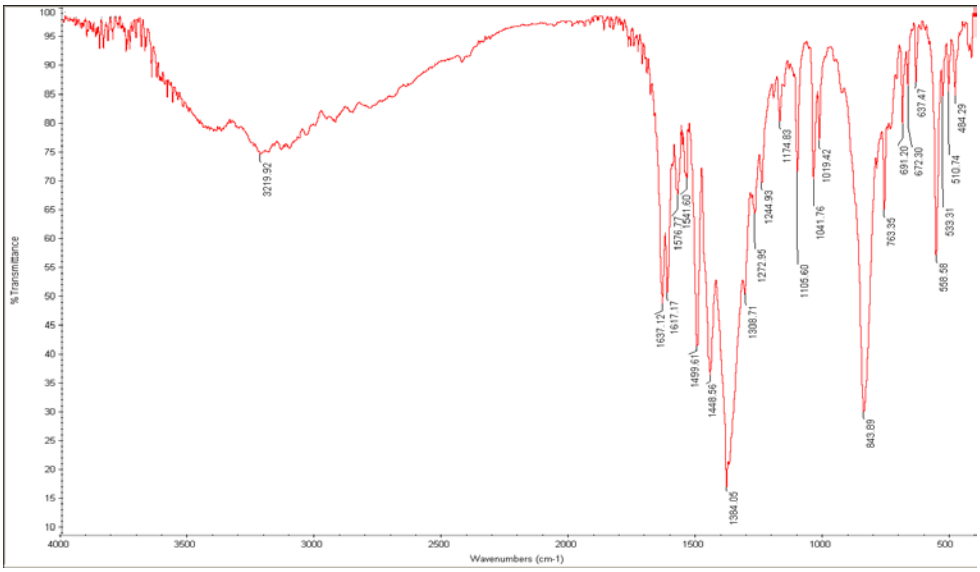
(B)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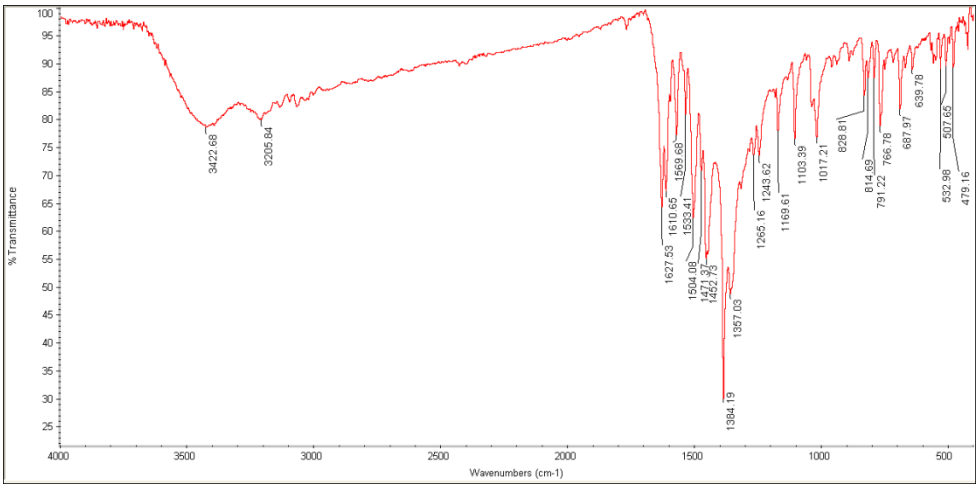
(C)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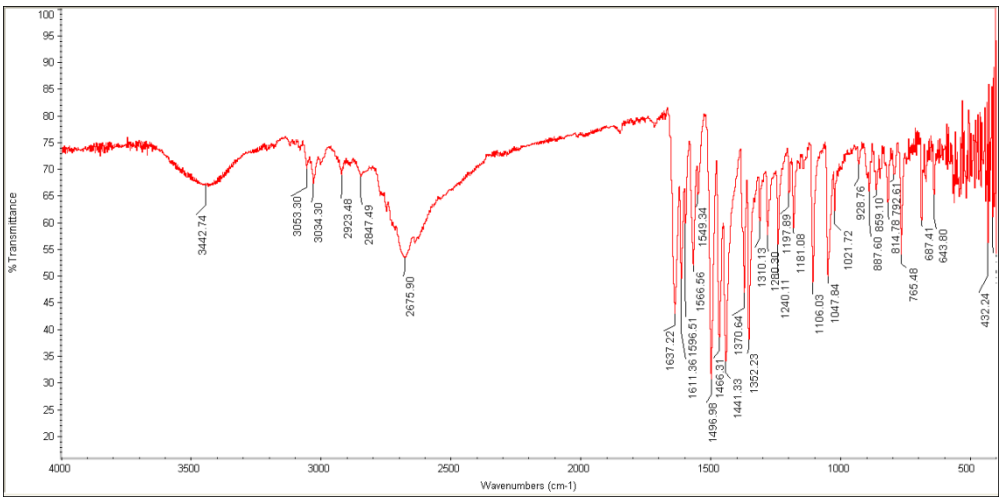
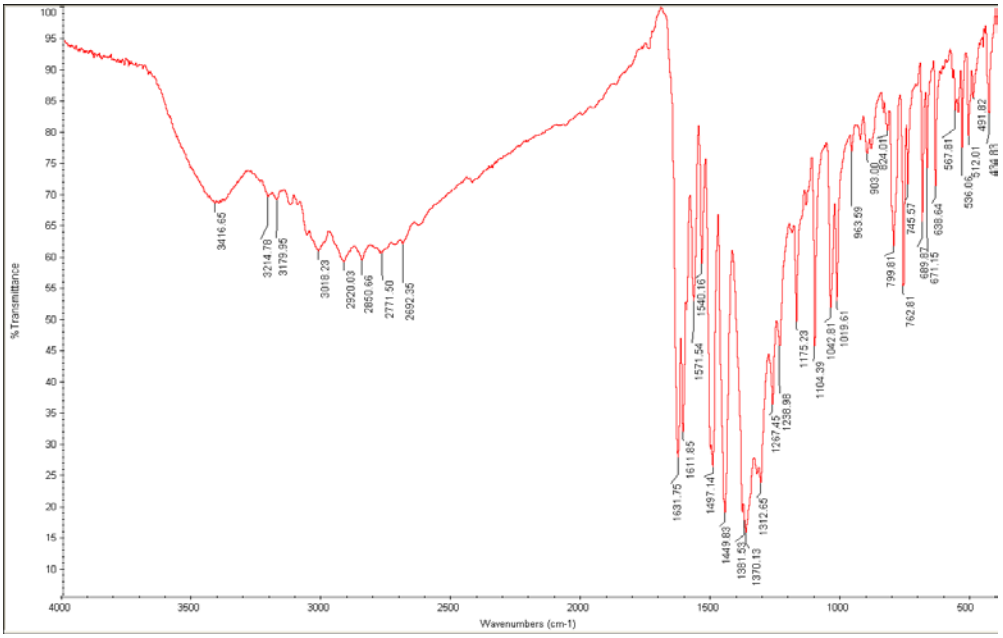
479.16

(D)



(E)



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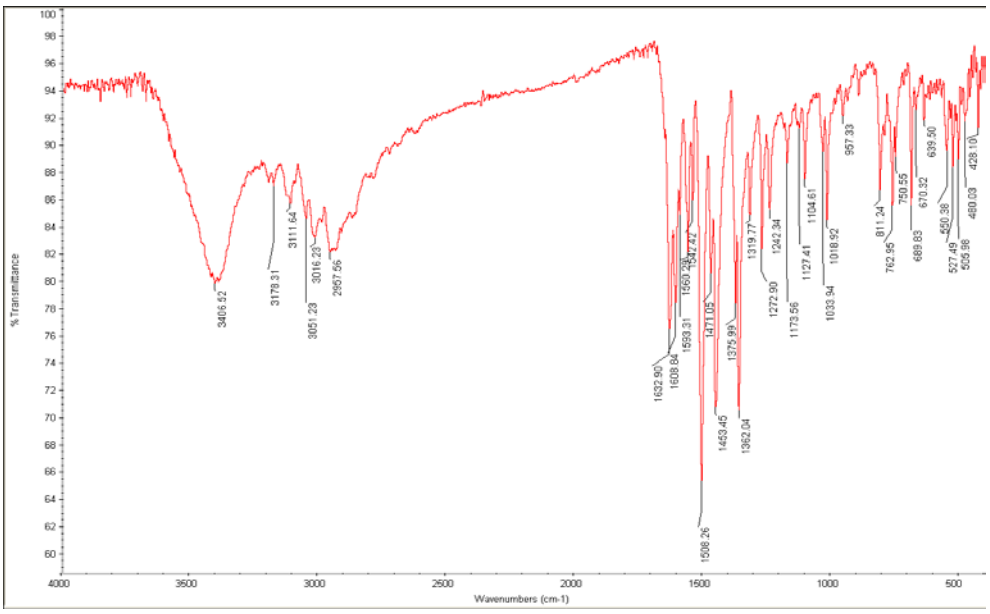


Figure S1. (A)-(F) IR spectra (KBr pellet) of complexes **1-6**, respectively.

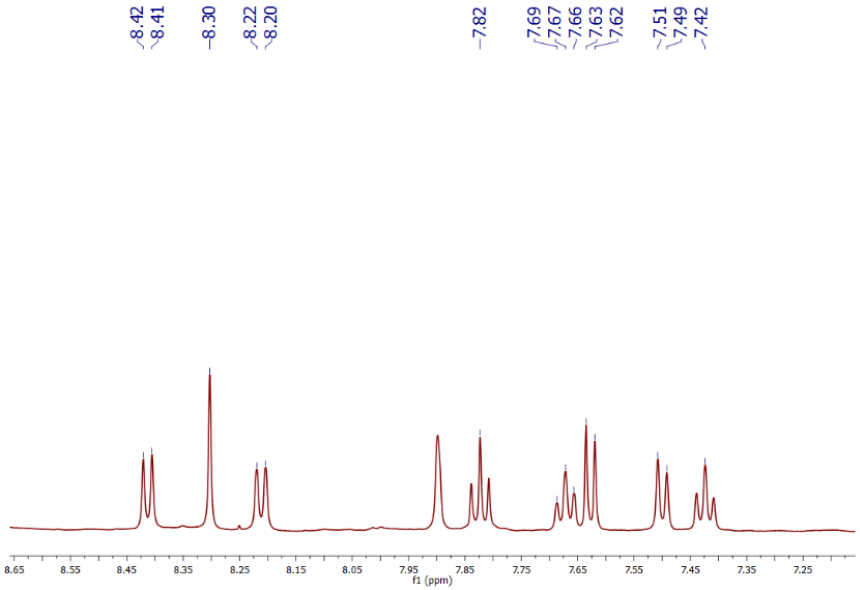


Figure S2. ^{1}H NMR spectrum of **L^{1}** in DMSO-d_6.

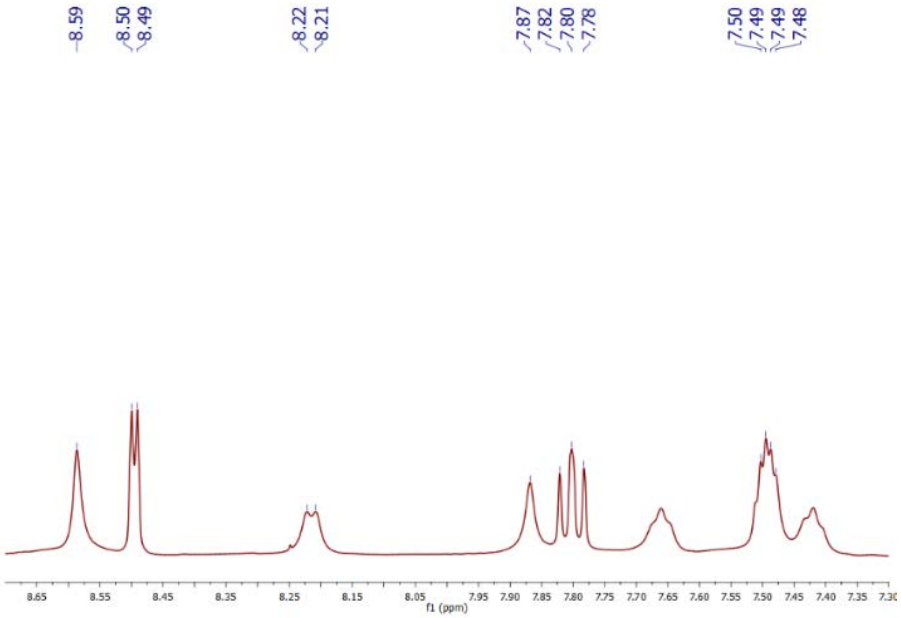


Figure S3. ^{1}H NMR spectrum of $\mathbf{L}^{2}$ in DMSO-d_6.

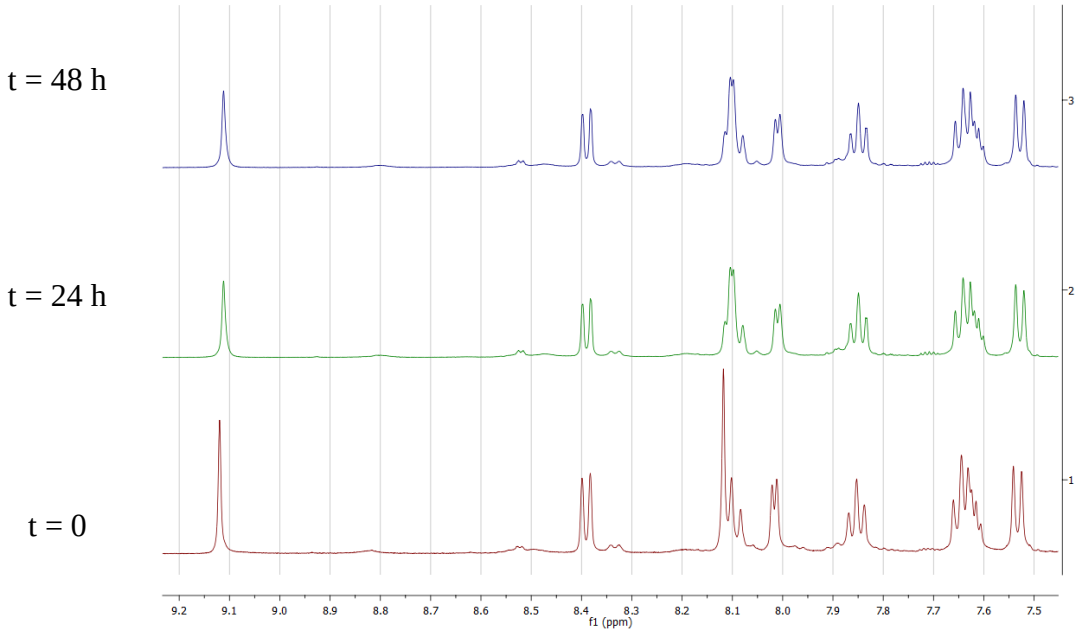


Figure S4. ^{1}H NMR spectra of complex **2** in DMSO-d_6 at three different times (0, 24 h and 48 h).

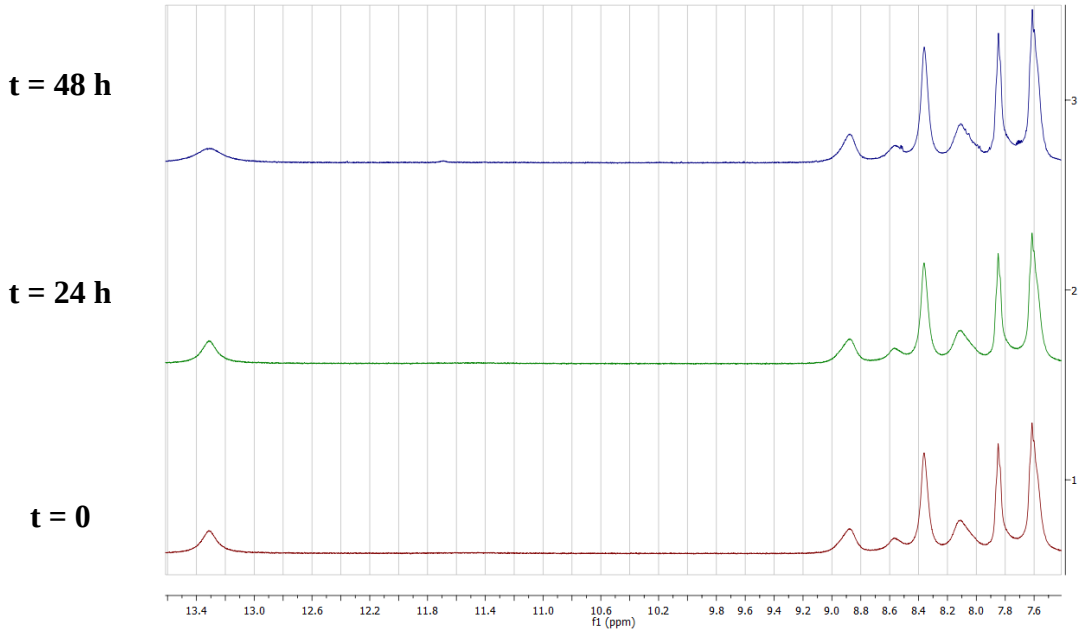


Figure S5. ^{1}H NMR spectra of complex **3** in DMSO-d_6 at three different times (0, 24 h and 48 h).

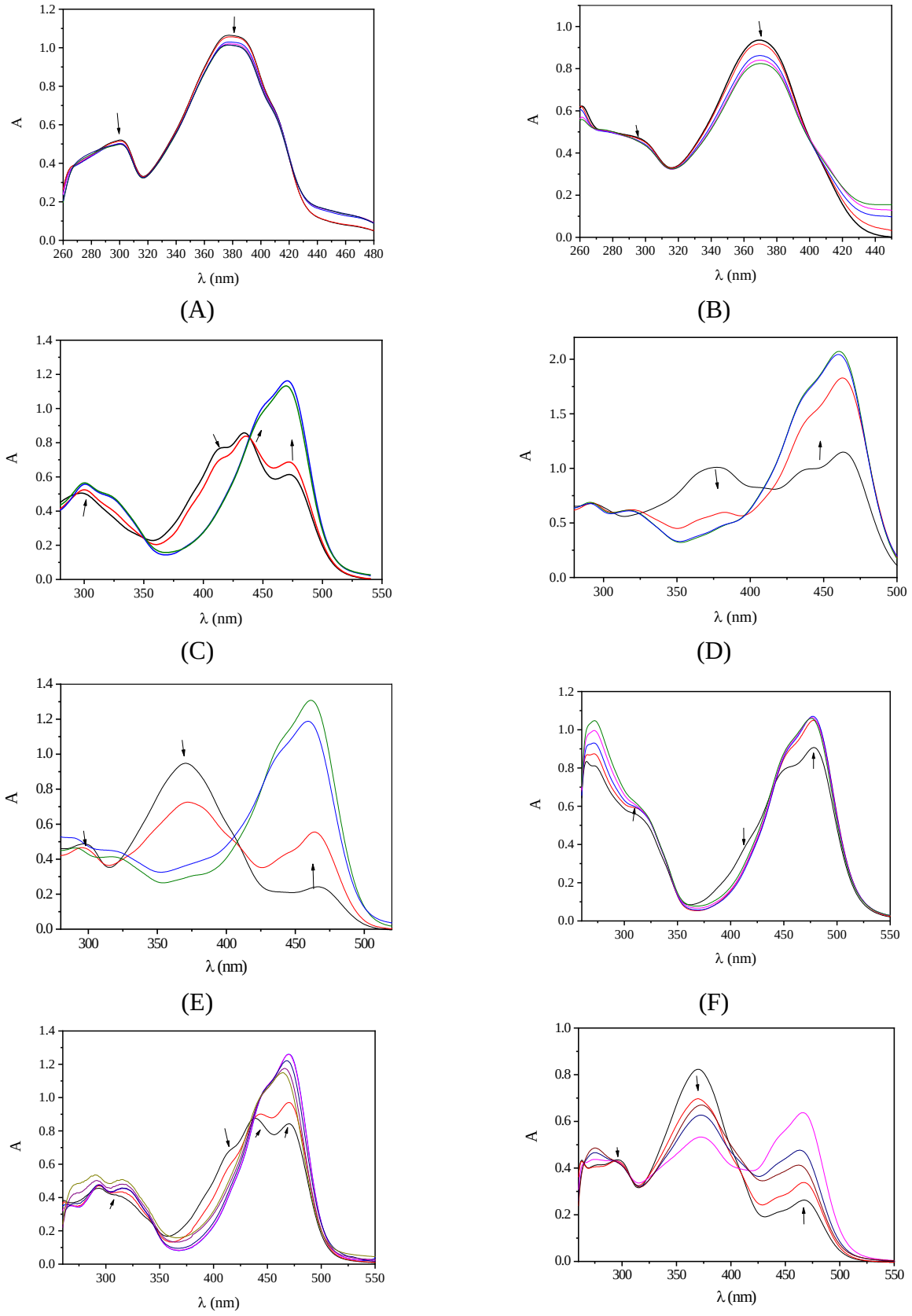


Figure S6. UV-vis spectra of DMSO solution of (A) $\mathbf{L}^{1}$ (100 µM)**,** (B) $\mathbf{L}^{2}$ (100 µM), (C) complex **1** (20 µM), (D) complex **2** (50 µM), (E) complex **3** (50 µM), (F) complex **4** (50 µM), (G) complex **5** (50 µM), and (H) complex **6** (30 µM) in the presence of increasing amounts of CT DNA. The arrows show the changes upon addition of CT DNA.

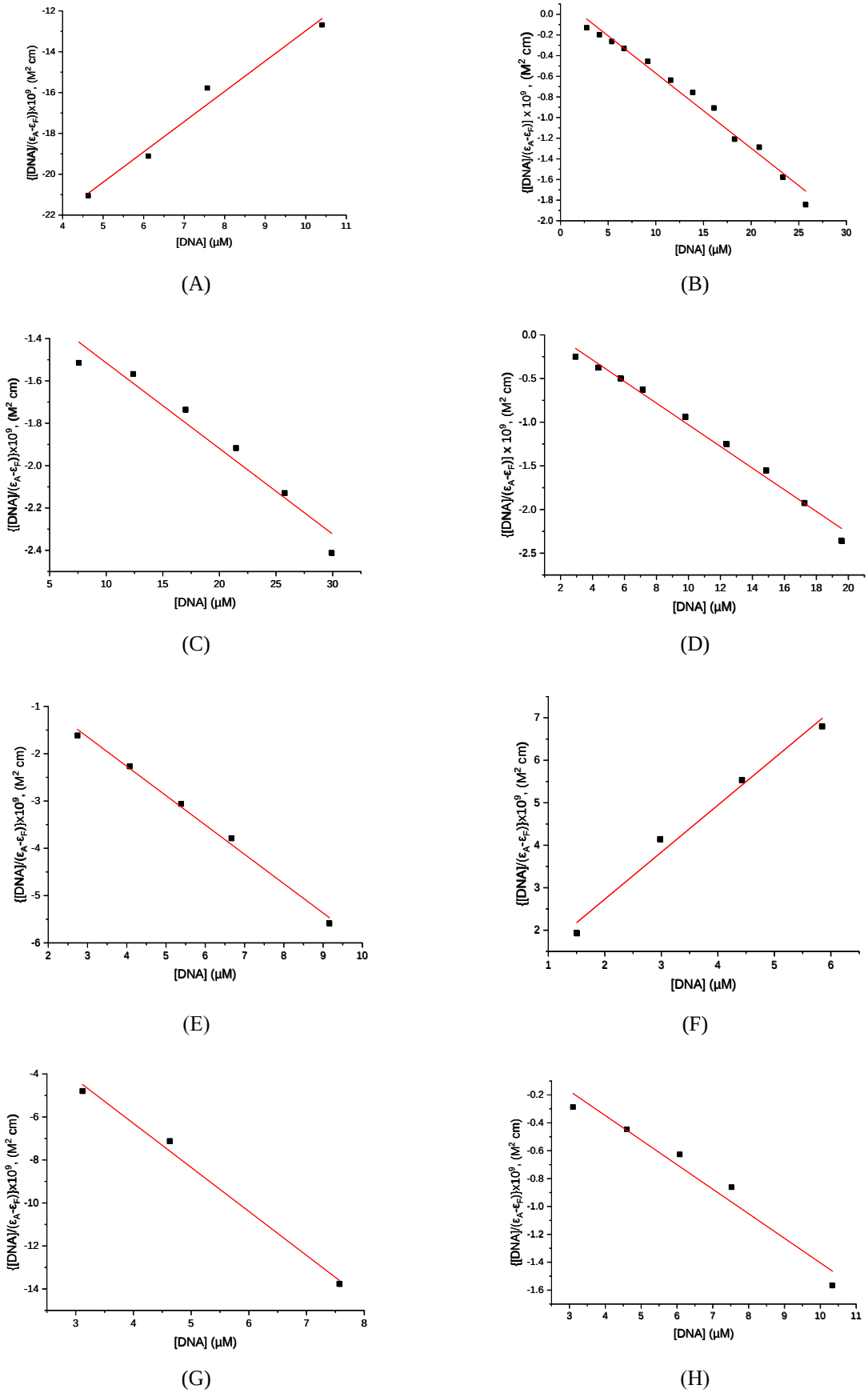
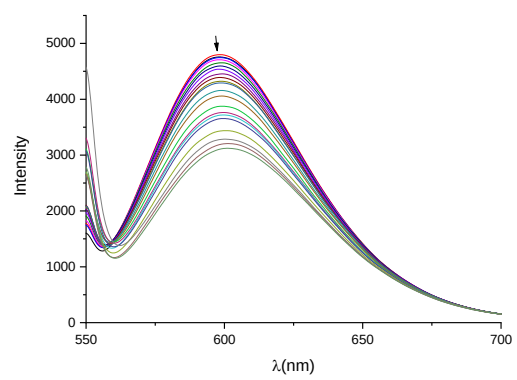


Figure S7. Plot of $\frac{[DNA]}{(\varepsilon_A - \varepsilon_f)}$ *versus* [DNA] for (A) $\mathbf{L^1}$**,** (B) complex **1**, (C) $\mathbf{L^2}$, (D) complex **2**, (E) complex **3**, (F) complex **4**, (G) complex **5** and (H) complex **6**.



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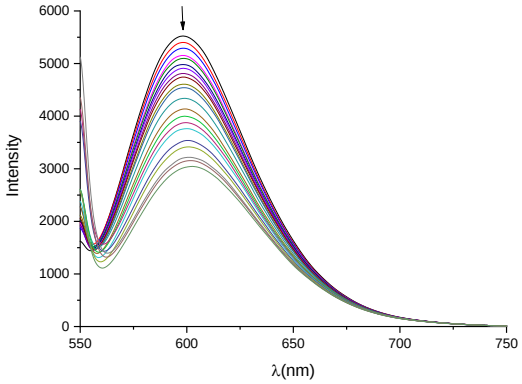

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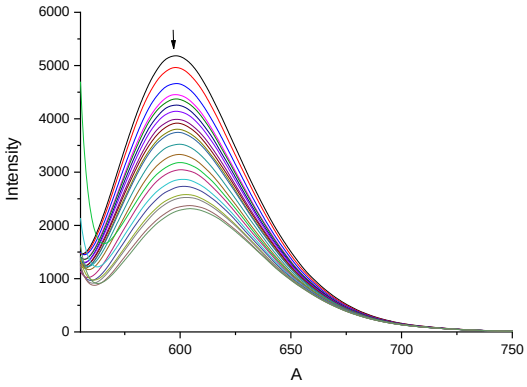

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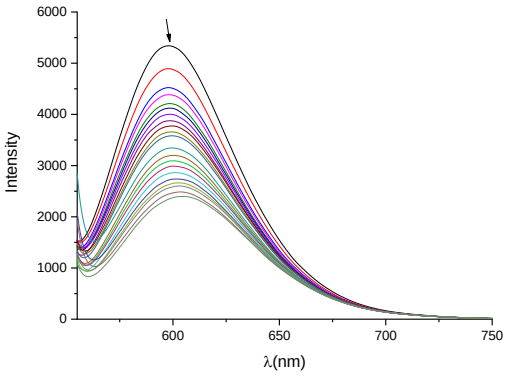

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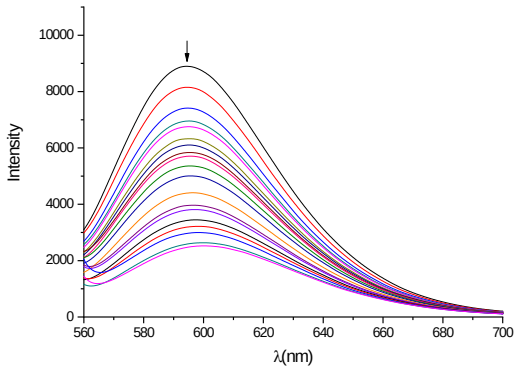


(E)

Figure S8. Fluorescence emission spectra (λ_{exc} = 540 nm) for EB-DNA ([EB] = 20 μM, [DNA] = 26 μM) in buffer solution in the absence and presence of increasing amounts (r = [complex] / [DNA] = 0 – 0.2) of (A) $[Ni(L^1)_2](NO_3)_2$ (complex **1)**, (B) $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$ (complex **3)**, (C) $[Cu(L^2)Cl_2]$ (complex **4)**, (D) $[Ni(L^2)_2](NO_3)_2$ (complex **5)** and (E) $[Mn(L^2)(CH_3OH)Cl_2]$ (complex **6)**. The arrow shows the changes of intensity upon increasing amounts of the complex**.**

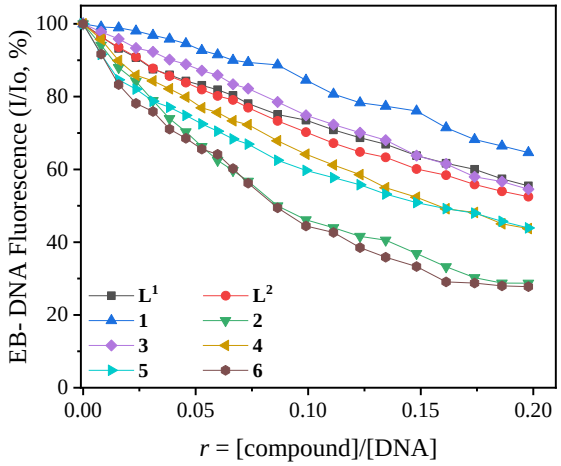


Figure S9. Plot of relative EB-DNA fluorescence intensity (I/Io, %) at λ_{em} = 592 nm *versus* r (r = [compound]/[DNA]) in buffer solution (150 mM NaCl and 15 mM trisodium citrate at pH 7.0) in the presence of the compounds (up to 55.5% of the initial EB-DNA fluorescence for **L**^{1}, 52.5% for **L**^{2}, 64.6% for complex **1**, 28.7% for complex **2**, 54.5% for complex **3**, 43.7% for complex **4**, 43.9% for complex **5** and 27.8% for complex **6)**.

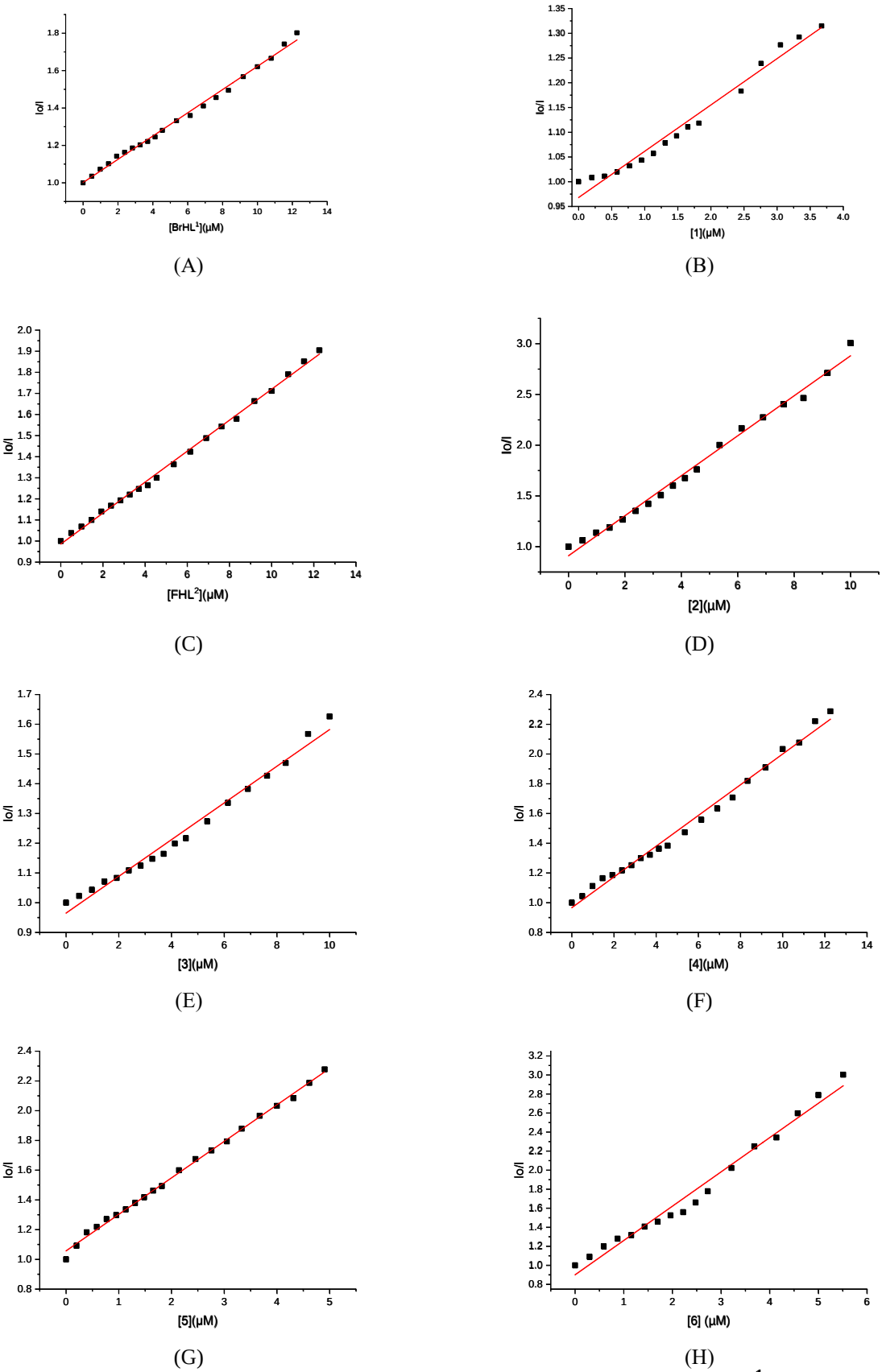


Figure S10. Stern-Volmer quenching plot of EB-DNA fluorescence for (A) $\mathbf{L^1}$, (B) complex **1**, (C) $\mathbf{L^2}$, (D) complex **2**, (E) complex **3**, (F) complex **4**, (G) complex **5** and (H) complex **6**.

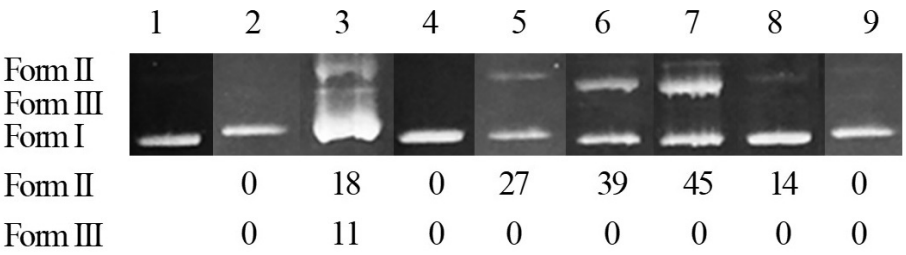
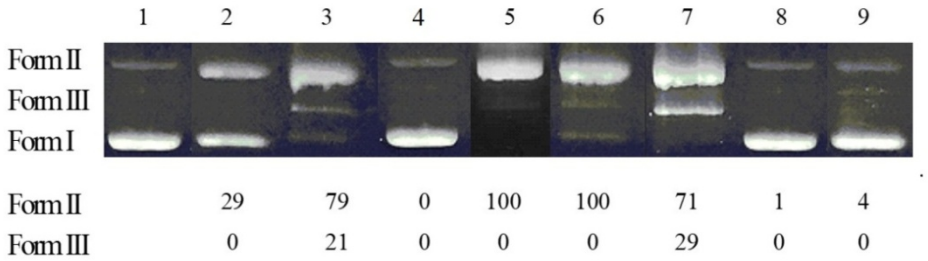


Figure S11. Agarose gel electrophoretic pattern of plasmid DNA (pBR322 DNA) with the compounds at 500 μM. Gel electrophoreses pictures: Lane 1: DNA (control); Lane 2: DNA + **L^1** (500 μM); Lane 3: DNA + $[Ni(L^1)_2](NO_3)_2$, **1** (500 μM); Lane 4: DNA + **L^2** (500 μM); Lane 5: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2** (500 μM); Lane 6: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3** (500 μM); Lane 7: DNA + $[Cu(L^2)Cl_2]$, **4** (500 μM); Lane 8: DNA + $[Ni(L^2)_2](NO_3)_2$, **5** (500 μM); Lane 9: DNA + $[Mn(L^2)(CH_3OH)Cl_2]$, **6** (500 μM). Bottom: Calculation of the % conversion to ss and ds damage. DNA forms: Form I = supercoiled, Form II = relaxed, Form III = linear plasmid DNA.



	1	2	3	4	5	6	7	8	9
Form II		29	79	0	100	100	71	1	4
Form III		0	21	0	0	0	29	0	0

Figure S12. Agarose gel electrophoretic pattern of plasmid DNA (pBR322 DNA) with the compounds at 500 μM upon irradiation at 312 nm. Top: Gel electrophoreses pictures: Lane 1: DNA irradiated (control); Lane 2: DNA + **L^{1}**; Lane 3: DNA + $[Ni(L^{1})_2](NO_3)_2$, **1**; Lane 4: DNA + **L^{2}**; Lane 5: DNA + $[Zn(L^{2})_2](NO_3)(PF_6)$, **2**; Lane 6: DNA + $[Cd(L^{2})(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3**; Lane 7: DNA + $[Cu(L^{2})Cl_2]$, **4**; Lane 8: DNA + $[Ni(L^{2})_2](NO_3)_2$, **5**; Lane 9: DNA + $[Mn(L^{2})(CH_3OH)Cl_2]$, **6**. Bottom: Calculation of the % conversion to ss and ds damage. DNA forms: Form I = supercoiled, Form II = relaxed, Form III = linear plasmid DNA.

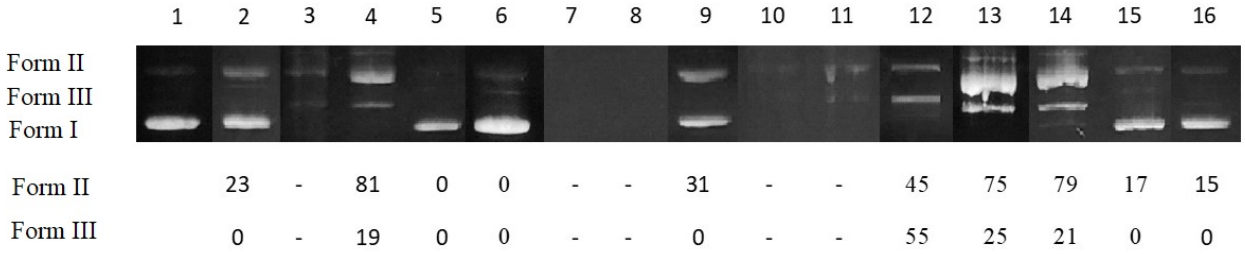
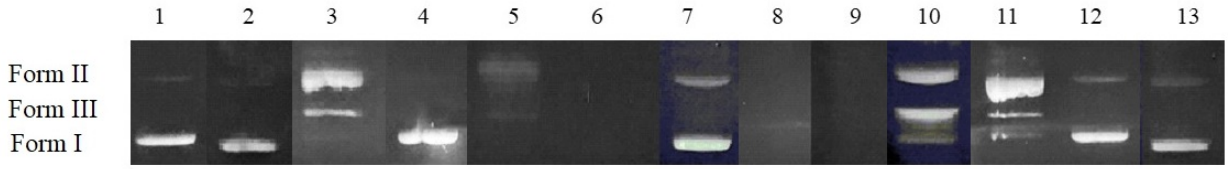


Figure S13. Agarose gel electrophoretic pattern of EB-stained plasmid DNA (pBR322DNA) with the compounds at various concentrations (100 – 500 μM) upon irradiation at 365 nm, after 60 min of electrophoresis. Top: Gel electrophoreses pictures: Lane 1: DNA irradiated (control); Lane 2: DNA + **L^1** (500 μM); Lane 3: DNA + $[Ni(L^1)_2](NO_3)_2$, **1** (500 μM); Lane 4: DNA + $[Ni(L^1)_2](NO_3)_2$, **1** (200 μM); Lane 5: DNA + $[Ni(L^1)_2](NO_3)_2$, **1** (100 μM); Lane 6: DNA + **L^2** (500 μM); Lane 7: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2 (**500 μM); Lane 8: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2 (**200 μM); Lane 9: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2 (**100 μM); Lane 10: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3 (**500 μM); Lane 11: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3 (**200 μM); Lane 12: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3 (**100 μM); Lane 13: DNA + **4 (**500 μM); Lane 14: DNA + $[Cu(L^2)Cl_2]$, **4 (**200 μM); Lane 15: DNA + $[Ni(L^2)_2](NO_3)_2$, **5 (**500 μM); Lane 16: DNA + $[Mn(L^2)(CH_3OH)Cl_2]$, **6 (**500 μM). Bottom: Calculation of the % conversion to ss and ds damage. DNA forms: Form I = supercoiled, Form II = relaxed, Form III = linear plasmid DNA.



	1	2	3	4	5	6	7	8	9	10	11	12	13
Form II		0	73	0	100	-	24	-	-	39	55	0	4
Form III		0	27	0	0	-	0	-	-	38	13	0	0

Figure S14. Agarose gel electrophoretic pattern of EB-stained plasmid DNA (pBR322DNA) with the compounds at various concentrations (100 – 500 μM) upon irradiation with visible light, after 60 min of electrophoresis. Top: Gel electrophoreses pictures: Lane 1: DNA irradiated (control); Lane 2: DNA + **L^1** (500 μM); Lane 3: DNA + $[Ni(L^1)_2](NO_3)_2$, **1** (500 μM); Lane 4: DNA + **L^2** (500 μM); Lane 5: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2** (500 μM); Lane 6: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2** (200 μM); Lane 7: DNA + $[Zn(L^2)_2](NO_3)(PF_6)$, **2 (**100 μM); Lane 8: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3 (**500 μM); Lane 9: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3 (**200 μM); Lane 10: DNA + $[Cd(L^2)(H_2O)(CH_3OH)(NO_3)](NO_3)$, **3 (**100 μM); Lane 11: DNA + $[Cu(L^2)Cl_2]$, **4 (**500 μM); Lane 12: DNA + $[Ni(L^2)_2](NO_3)_2$, **5 (**500 μM); Lane 13: DNA + $[Mn(L^2)(CH_3OH)Cl_2]$, **6 (**500 μM). Bottom: Calculation of the % conversion to ss and ds damage. DNA forms: Form I = supercoiled, Form II = relaxed, Form III = linear plasmid DNA.

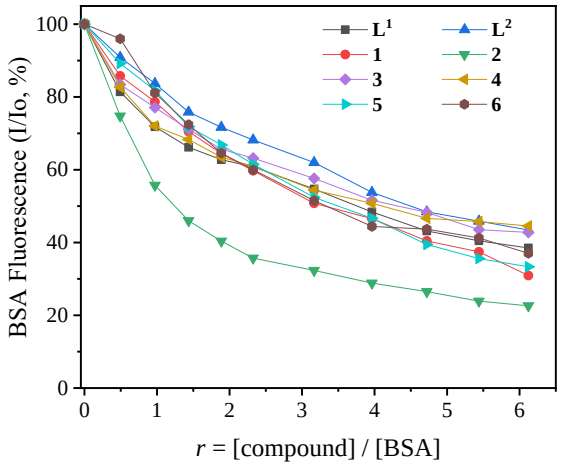
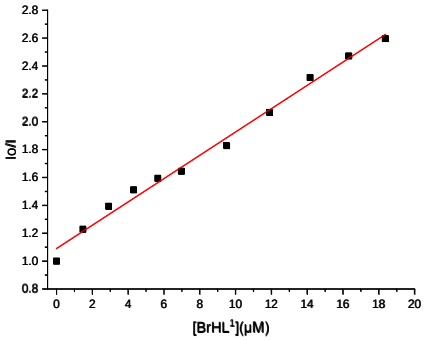
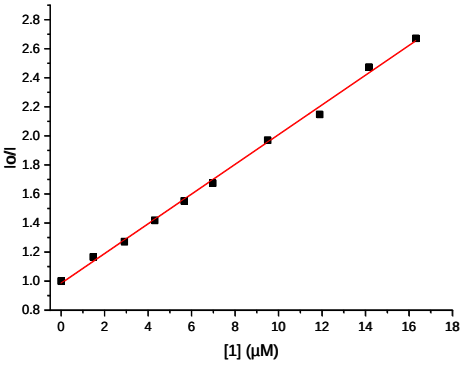


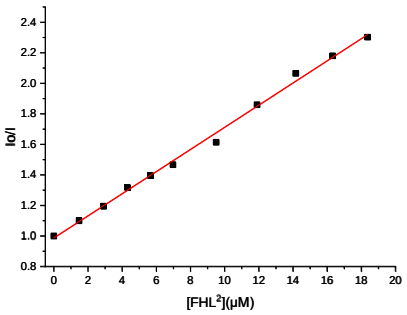
Figure S15. Plot of relative BSA-fluorescence intensity (I/Io, %) at $\lambda_{emission}$ = 343 nm *versus* *r* (*r* = [compound]/[BSA]) for the compounds (up to 38.5% of the initial BSA fluorescence for **L**^{1}, 43.9% for **L**^{2}, 31.0% for **1**, 22.6% for **2**, 42.8% for **3**, 44.5% for **4,** 33.3% for **5** and 37.0% for **6**) in buffer solution (150 mM NaCl and 15 mM trisodium citrate at pH 7.0).



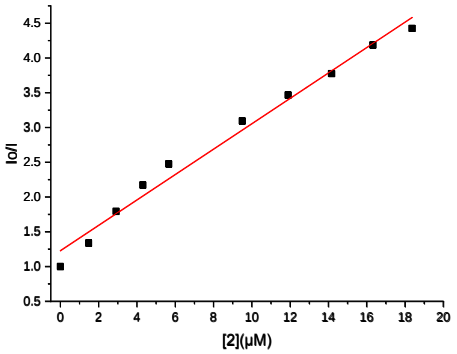
(A)



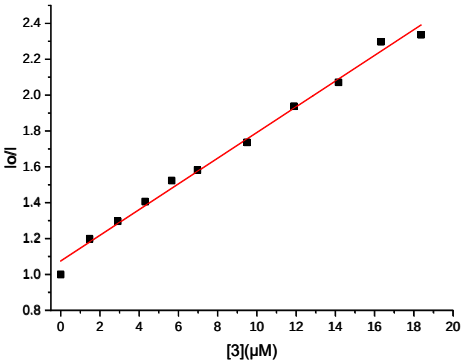
(B)



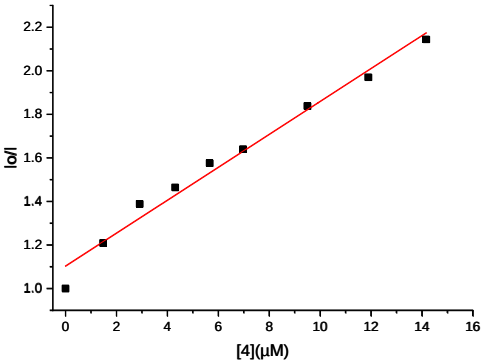
(C)



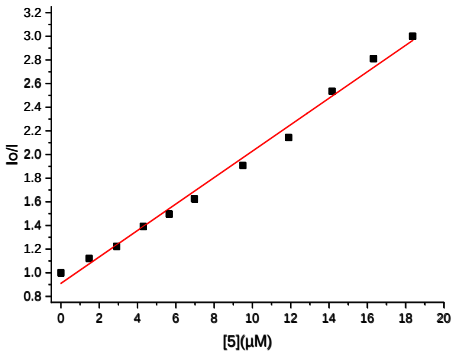
(D)



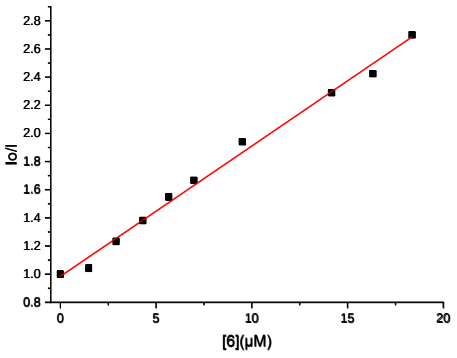
(E)



(F)

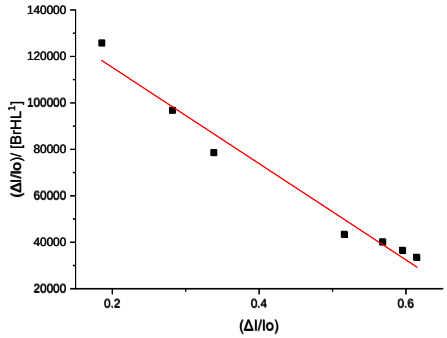


(G)

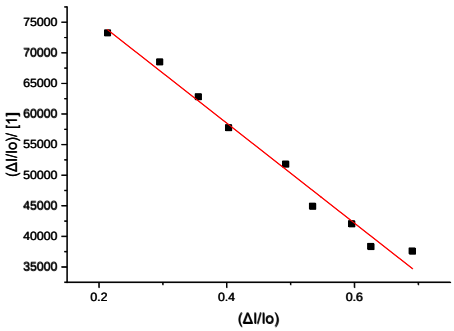


(H)

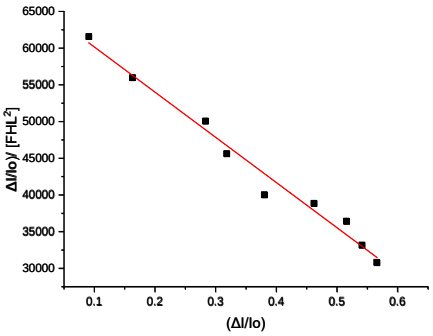
Figure S16. Stern-Volmer quenching plot of BSA fluorescence for (A) $\mathbf{L^1}$, (B) complex **1**, (C) $\mathbf{L^2}$, (D) complex **2**, (E) complex **3**, (F) complex **4**, (G) complex **5** and (H) complex **6**.



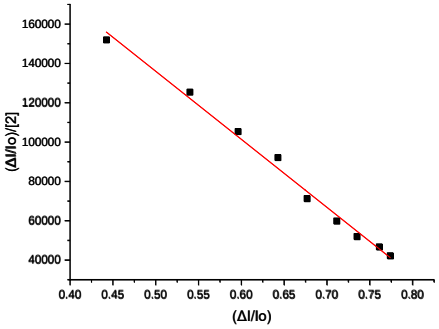
(A)



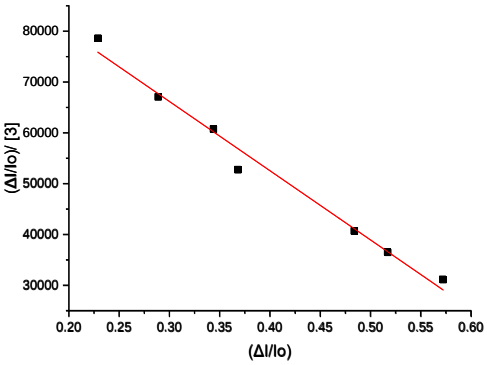
(B)



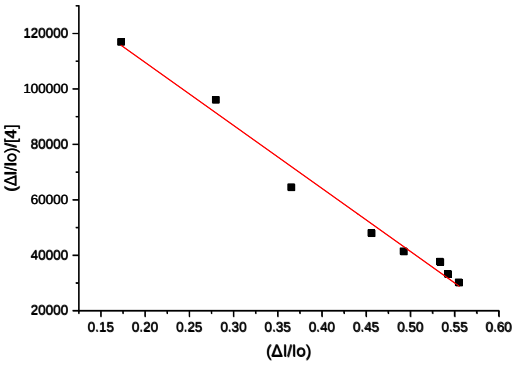
(C)



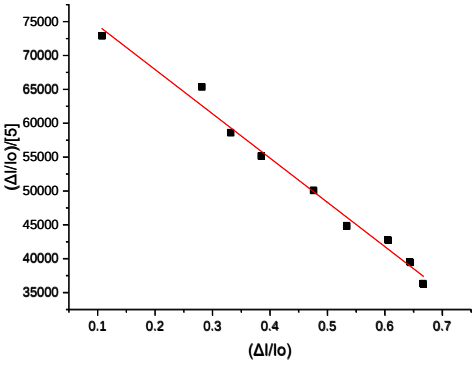
(D)



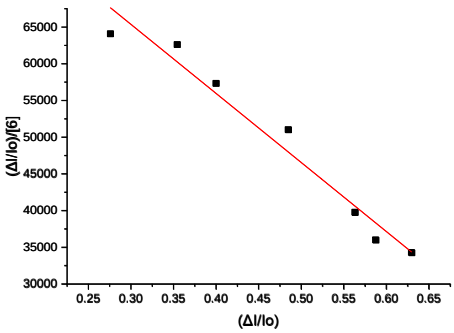
(E)



(F)



(G)



(H)

Figure S17. Scatchard plot of BSA for (A) $\mathbf{L^1}$**,** (B) complex **1**, (C) $\mathbf{L^2}$, (D) complex **2**, (E) complex **3**, (F) complex **4**, (G) complex **5** and (H) complex **6**.

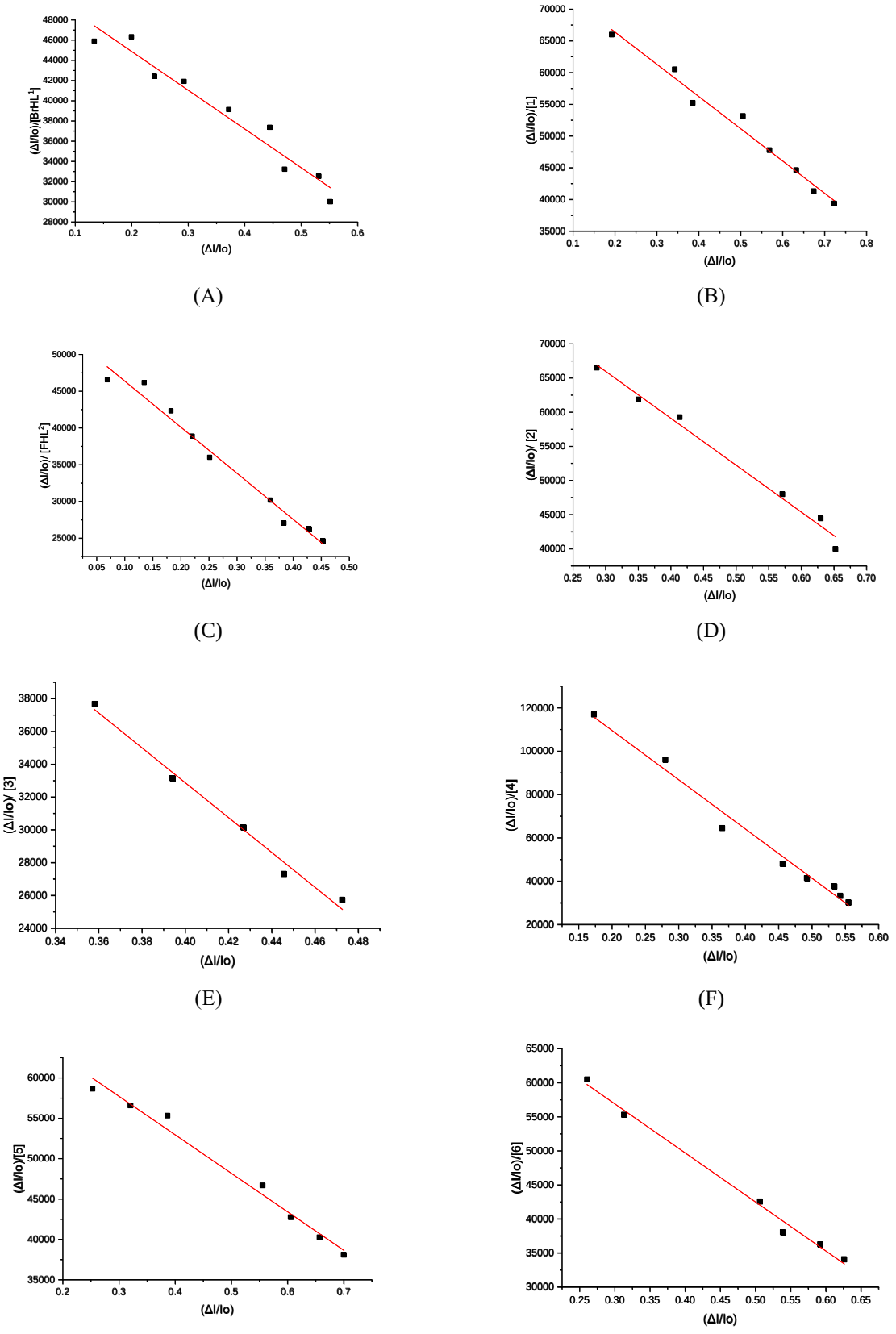


Figure S18. Scatchard plot of BSA-warfarin for (A) $\mathbf{L^1}$, (B) complex **1**, (C) $\mathbf{L^2}$, (D) complex **2**, (E) complex **3**, (F) complex **4**, (G) complex **5** and (H) complex **6**.

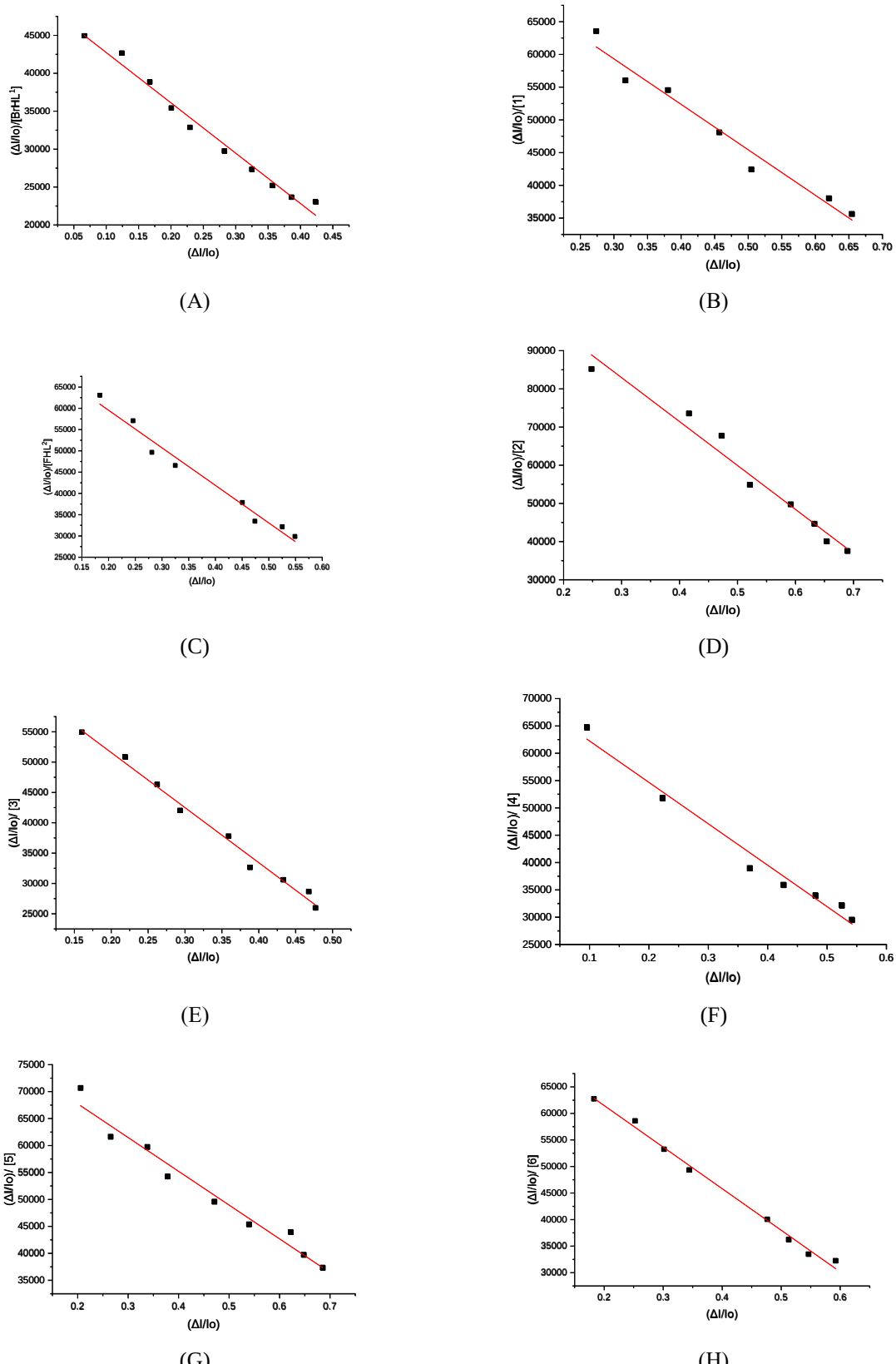


Figure S19. Scatchard plot of BSA-ibuprofen for (A) $\mathbf{L^1}$, (B) complex **1**, (C) $\mathbf{L^2}$, (D) complex **2**, (E) complex **3**, (F) complex **4**, (G) complex **5** and (H) complex **6**.

Table S1. Crystallographic data, data collection and refinement details for complexes **1-6**.

	1	**2**	**3**	**4**	**5**	**6**
Crystal data						
Chemical formula	$C_{28.5}H_{24}Br_2N_{12}NiO_{7.5}$	$C_{28.5}H_{22}F_8N_{11}O_{3.5}P_1Zn_1$	$C_{15}H_{16}CdFN_7O_8$	$C_{14}H_{10}Cl_2CuFN_5$	$C_{28.25}H_{22}F_2N_{12}NiO_{6.75}$	$C_{16}H_{18}Cl_2FMnN_5O_2$
M_r	873.1	822.9	553.73	401.72	734.27	457.18
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*C*2/*c*	$P2_1/n$	*C*2/*c*	$P2_1/n$	*C*2/*c*	$P2_1/n$
Temperature (K)	295	295	295	295	295	295
a (Å)	20.3724(17)	10.3840(5)	13.149(6)	7.802(4)	16.205(6)	11.961(4)
b (Å)	10.6925(9)	27.3190(15)	15.905(7)	14.426(9)	16.629 (6)	8.170(3)
c (Å)	15.7430(13)	12.0585(7)	19.736(9)	13.723(8)	23.492(7)	20.759(8)
β (°)	95.850(2)	101.9964(19)	97.53(2)	94.399(15)	104.765(10)	103.555(11)
V ($Å^3$)	3411.5(5)	3346.1(3)	4092(3)	1539.9(15)	6122(4)	1972.1(12)
Z	4	4	8	4	8	4
Radiation type	Mo*K*α	MoKα	Mo*K*α	Mo*K*α	Mo*K*α	Mo*K*α
μ (mm^{-1})	2.98	0.88	1.14	1.78	0.71	0.97
Crystal size (mm)	0.21 × 0.14 × 0.13	0.23 × 0.22 × 0.16	0.23 × 0.22 × 0.16	0.22 × 0.17 × 0.16	0.22 × 0.19 × 0.15	0.22 × 0.19 × 0.14
Data collection						
Diffractometer	Bruker Kappa Apex2					
Absorption correction	Numerical, Analytical Absorption (De Meulenaer&Tompa, 1965)					
T_{min}, T_{max}	0.66, 0.68	0.83, 0.87	0.78, 0.83	0.74, 0.75	0.87, 0.90	0.83, 0.87
Measured, Independent, Observed [$I > 2.0\sigma(I)$] reflections	9756, 3186, 2414	34148, 6355, 4859	22737, 4170, 3542	10474, 2913, 2158	47841, 5835, 4600	20642, 3753, 2796
$R_{int,}$ $(\sin\theta/\lambda)_{max}$ ($Å^{-1}$)	0.021, 0.617	0.015, 0.611	0.030, 0.626	0.058, 0.613	0.038, 0.612	0.037, 0.612
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.038, 0.062, 1.00	0.042, 0.085, 1.00	0.033, 0.052, 1.00	0.046, 0.077, 1.00	0.052, 0.074, 1.00	0.041, 0.065, 1.00
No. of reflections, parameters, restraints	2414, 234, 1	4859, 471, 1	3542, 289, 6	2158, 208,-	4600, 450, 5	2796, 244, -
H-atom treatment	H-atom parameters constrained					
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.87, −0.61	0.58, −0.40	0.63, −1.75	0.54, −0.45	0.51, −0.47	0.47, −0.37

Table S2. Hydrogen-bond geometry (Å, º) for complexes **1-6**.

D-H⋯A	**D-H** (Å)	**H…A** (Å)	**D…A** (Å)	**D-H-A** (º)	**Symmetry code**
1					
N2—H21⋯O2^{ii}	0.86	2.37	3.147 (8)	151	(ii) −*x*+3/2, *y*+1/2, −*z*+3/2
N2—H21⋯O3^{ii}	0.86	2.10	2.906 (8)	157	(iii) −*x*+1, −*y*+1, −*z*+1
O4—H42⋯O3^{iii}	0.82	2.34	3.162 (8)	179	(iv) *x*−1/2, *y*+1/2, *z*.
O4—H43⋯O3^{iv}	0.87	1.76	2.589 (8)	159	
2					
N2—H21⋯O4^{i}	0.85	1.88	2.684 (6)	158	(i) −x+1, −y+1, −z
N7—H71⋯N11^{ii}	0.84	2.54	3.357 (6)	166	(ii) −x+1, −y+1, −z+1
N7—H71⋯O2^{ii}	0.84	2.41	3.099 (6)	140	
N7—H71⋯O3^{ii}	0.84	1.98	2.795 (6)	166	
O4—H294⋯N11	0.83	2.47	3.239 (6)	154	
O4—H294⋯O2	0.83	1.79	2.621 (6)	180	
3					
N2—H21⋯O6^{i}	0.83	2.40	3.181 (5)	157	(i) −x+1/2, y+1/2, −z+3/2
N2—H21⋯O8^{i}	0.83	2.07	2.802 (5)	147	(ii) x, −y+1, z−1/2
O4—H42⋯N7^{ii}	0.85	2.59	3.414 (5)	163	(iii) −x+1, y, −z+3/2
O4—H42⋯O8^{ii}	0.85	1.86	2.704 (5)	168	(iv) −x+1, −y+1, −z+1
O5—H52⋯N3^{iii}	0.85	1.99	2.822 (5)	165	
O5—H53⋯O2^{iv}	0.86	1.91	2.759 (5)	168	
5					
N2—H21⋯O9^{iii}	0.87	2.04	2.827 (6)	150	(i) −x+1, y, −z+3/2
N7—H71⋯O1^{i}	0.85	2.21	3.019 (6)	159	(ii) −x, −y+1, −z+1
N7—H71⋯O3^{i}	0.85	2.20	2.945 (6)	145	(iii) −x+1/2, −y+1/2, −z+1
O9—H92⋯O7^{ii}	0.82	2.06	2.636 (6)	127	(iv) −x+1/2, y+1/2, −z+3/2
O10—H103⋯N11^{iv}	0.85	2.20	2.978 (6)	152	(vi) −x+1/2, −y+3/2, −z+1
O10—H103⋯O3^{iv}	0.85	1.76	2.612 (6)	175	
O10^{vi}—H294⋯O10	0.86	1.73	2.464 (6)	142	
6					
O1—H11⋯O2	0.81	1.88	2.686 (5)	174	

Table S3. Binding interactions of complex **1** with DNA

Complex 1 interacting atom	Nucleobase	Number of Nucleobase	Type of atom	Bond length (Å)
H21	DG	10	OP2	2.140
HN3	DC	13	N4	2.404
H9	DC	13	H5	1.800
C5	DG	110	O6	3.014
N2	DG	10	OP2	2.963
H9	DC	13	C5	2.575
H6	DC	13	N4	2.561
H5	DG	110	O6	2.424
C2	DG	10	H2'	2.660
HN3	DC	13	H42	1.970
H21	DG	10	P	2.877
N3	DC	13	H42	2.679
N3	DC	13	N4	3.306
C6	DG	110	O6	3.242
N3	DG	12	N7	3.323
C2	DG	10	C2'	3.483
C9	DC	13	H5	2.791
C9	DG	12	C8	3.500
C6	DC	13	N4	3.426
C9	DG	12	H8	2.808
N2	DG	10	P	3.618
HN3	DG	12	N7	2.760
N2	DG	10	H2'	2.773
H5	DG	110	C6	2.872
H3	DG	10	OP2	2.692
C7	DG	10	C2'	3.607
C3	DG	10	H8	2.913
C9	DC	13	C5	3.632
N2	DG	10	O5'	3.371
C3	DG	10	C8	3.667
C4	DG	10	C8	3.669
C3	DG	10	OP2	3.472
N2	DG	10	C2'	3.615
H9	DG	12	C8	2.991
C1	DG	10	H3'	3.015
H6	DC	13	H41	2.322
C3	DG	10	H2'	3.032
HN3	DC	13	C4	3.035
C5	DG	110	C6	3.746
C11	DG	12	H2'	3.048
C7	DG	10	H2"	3.058
C6	DC	13	H41	3.059
N3	DG	12	C8	3.698
C1	DG	10	C2'	3.798
C11	DG	12	C2'	3.798

Table S4. Binding interactions of complex **2** with DNA.

Complex 2 interacting atom	Nucleobase	Number of Nucleobase	Type of atom	Bond length (Å)
C26	DA	109	C6	0.513
C25	DA	109	C5	0.986
C28	DG	110	C6	1.072
C25	DA	109	C6	1.104
C28	DG	110	O6	0.938
H26	DA	109	N1	0.400
C24	DA	109	N7	1.178
C26	DA	109	N1	1.291
C27	DG	110	C6	1.440
C26	DA	109	C5	1.552
H28	DG	110	C6	0.874
C26	DA	109	N6	1.508
C25	DA	109	N6	1.576
C25	DA	109	N7	1.578
C23	DA	109	N7	1.578
C28	DG	110	C5	1.691
C24	DA	109	C5	1.751
H26	DA	109	C6	1.052
C27	DA	109	C6	1.872
C27	DG	110	O6	1.707
N10	DG	110	O6	1.767
C27	DG	110	C5	2.149
H27	DG	110	N1	1.375
H28	DG	110	O6	1.242
C27	DG	110	N1	2.087
H28	DG	110	C5	1.471
F2	DA	109	C5	1.769
F2	DA	108	C5	1.780
C6	DC	111	H42	1.502
C26	DA	109	C2	2.228
C27	DA	109	N1	2.178
C5	DG	112	O6	2.046
H27	DG	110	C6	1.577
C6	DG	112	O6	2.073
F2	DA	109	C6	1.886
C28	DG	110	N7	2.237
F2	DA	108	C4	1.909
C24	DA	109	C6	2.346
C25	DA	109	C4	2.352
C25	DA	109	H62	1.655
C24	DA	109	C8	2.375
H26	DA	109	C2	1.688
C26	DA	109	C4	2.406
N10	DA	109	N7	2.263
C27	DA	109	N6	2.339
C27	DA	109	C5	2.418
C23	DA	109	C8	2.426
F2	DA	108	N7	1.961
N10	DG	110	C6	2.387
H5	DG	112	O6	1.563
C28	DG	110	N1	2.413
F2	DA	108	C8	2.072
C25	DA	109	N1	2.422
C6	DC	111	N4	2.456
C24	DA	109	N6	2.456
H6	DG	112	O6	1.622
F2	DA	109	N7	2.079

HN3	DC	11	H42	1.179
F2	DA	108	N9	2.088
N10	DG	110	N7	2.458
N10	DA	109	C5	2.558
H6	DC	111	H42	1.237
H5	DG	112	C6	1.962
F2	DA	109	N6	2.173
H26	DA	109	N6	1.931
H6	DC	111	N4	1.936
C24	DA	109	H62	2.013
N10	DG	110	C5	2.639
C25	DA	109	C8	2.733
H23	DA	109	N7	1.962
N9	DA	109	N7	2.589
C28	DA	109	C6	2.755
N1	DG	110	N7	2.630
C28	DA	109	C5	2.782
C26	DG	110	C6	2.783
C5	DC	111	H5	2.092
C26	DA	109	N7	2.717
C23	DA	109	C5	2.806
H27	DG	110	C2	2.111
HN3	DC	11	N4	2.048
C26	DA	109	H61	2.130
H5	DG	112	N7	2.055
H5	DG	112	C5	2.132
C27	DA	109	C2	2.843
C26	DA	109	N3	2.782
H28	DG	110	N1	2.088
C5	DG	112	C6	2.864
N3	DC	11	H42	2.134
C26	DG	110	O6	2.693
H26	DA	109	C5	2.220
C4	DG	110	H2"	2.220
C1	DG	110	N7	2.848
C26	DA	109	H62	2.223
C3	DG	110	C2'	2.927
C24	DG	110	O6	2.715
C5	DC	111	C5	2.936
H23	DA	108	C8	2.251
C24	DA	109	C4	2.956
C7	DC	111	H42	2.258
C8	DG	110	N7	2.888
C28	DG	110	C4	2.991
C2	DG	110	C8	2.994
N2	DG	110	C8	2.927
C25	DA	108	C5	3.005
H27	DG	110	C5	2.314
C1	DG	110	C8	3.014
C27	DG	110	C4	3.024
N10	DA	109	C6	2.951
H28	DG	110	N7	2.253
H6	DC	11	N4	2.255
C27	DG	110	C2	3.032
C28	DA	109	N6	2.959
C27	DA	109	C4	3.039
C5	DG	112	N7	2.979
C27	DG	110	N7	3.000
C5	DC	111	H42	2.391
C3	DG	110	H2"	2.396

N2	DG	110	H8	2.326
H9	DC	11	H5	1.729
H6	DC	11	H41	1.736
C25	DA	108	C4	3.147
C25	DA	109	C2	3.149
C4	DG	110	C2'	3.153
N9	DA	109	C8	3.080
C23	DA	108	C8	3.155
F2	DA	108	C6	2.739
H27	DA	109	N1	2.387
N10	DA	109	C8	3.092
C25	DA	108	N7	3.094
N10	DA	109	N6	3.027
C28	DA	109	N7	3.108
C25	DA	109	N9	3.118
C4	DC	111	H5	2.494
N3	DC	11	N4	3.052
H27	DG	110	O6	2.283
C7	DG	110	C8	3.206
C27	DG	110	H1	2.508
C3	DG	110	H2'	2.509
C5	DG	112	C5	3.211
C5	DC	111	N4	3.138
C25	DA	108	C8	3.214
F2	DA	109	C4	2.801
H26	DT	14	H3	1.843
H27	DG	110	H1	1.847
C6	DG	112	C6	3.255
C6	DC	111	C4	3.256
C25	DA	109	H61	2.562
C26	DG	110	C5	3.271
C25	DG	110	O6	3.056
F1	DG	10	H2"	2.167
C6	DC	111	C5	3.289
C24	DA	109	N9	3.223
C23	DA	109	H8	2.599
F2	DA	109	H62	2.180
C7	DC	111	N4	3.244
N1	DG	110	C8	3.247
H27	DA	109	C6	2.637
C25	DA	109	N3	3.268
H28	DG	110	C4	2.647
H23	DA	108	H8	1.949
C25	DA	108	N9	3.274
C24	DG	110	C6	3.355
C6	DC	111	H5	2.655
C7	DG	110	N7	3.286
C1	DG	110	H8	2.669
H23	DA	109	C8	2.671
F2	DA	108	N3	2.881
C8	DG	110	C8	3.377
C24	DG	110	N7	3.306
C6	DC	11	N4	3.312
C26	DT	14	H3	2.687
C27	DA	109	N7	3.320
C27	DA	109	N3	3.320
H9	DC	11	C5	2.706
C2	DG	110	H8	2.706
F2	DA	109	N1	2.918
N7	DG	10	OP2	3.140

H26	DA	109	C4	2.722
C8	DG	110	C5	3.426
H26	DA	109	N3	2.653
C5	DC	111	C4	3.430
H27	DG	110	C4	2.730
C9	DG	12	O6	3.215
C28	DG	110	C8	3.439
N2	DG	110	N7	3.298
C26	DG	110	N1	3.374
C27	DA	109	H61	2.753
C28	DC	13	H41	2.755
F2	DA	109	C8	3.044
C28	DG	110	C2	3.475
C6	DC	11	H41	2.776
C4	DG	112	N7	3.406
N10	DA	109	H62	2.706
F1	DG	12	N7	2.992
C9	DC	11	H5	2.791
H5	DC	111	C5	2.795
C25	DG	110	C6	3.496
F1	DG	10	C2'	3.076
C2	DG	110	C2'	3.501
C8	DC	111	H42	2.808
C28	DA	109	C4	3.509
N3	DC	111	N4	3.360
H23	DA	108	N9	2.737
N3	DG	12	O6	3.230
C28	DA	109	N1	3.451
C23	DA	109	H62	2.829
H27	DG	110	N3	2.770
H6	DG	112	C6	2.846
C4	DC	111	C5	3.553
C2	DG	110	N7	3.479
C27	DG	110	N3	3.484
C9	DC	11	H42	2.863
N4	DG	110	O6	3.273
N3	DC	111	H42	2.796
H26	DA	109	H61	2.171
C27	DA	109	H62	2.872
N10	DA	109	C4	3.499
H9	DG	12	O6	2.660
C23	DA	109	C6	3.586
C24	DG	110	C5	3.587
C26	DA	108	C5	3.590
HN3	DG	12	O6	2.673
C5	DG	110	H2"	2.894
C24	DA	108	C8	3.595
C4	DG	112	O6	3.375
C27	DC	13	H41	2.900
H6	DC	11	H42	2.207
H26	DT	14	N3	2.832
H27	DA	109	C2	2.908
H9	DC	11	H42	2.211
C28	DG	110	H1	2.913
H5	DC	111	H5	2.219
C23	DA	109	N6	3.545
HN3	DC	111	N4	2.850
C23	DA	108	N9	3.551
C25	DA	108	C6	3.629
C26	DA	109	C8	3.630

C6	DG	10	O6	3.417
C26	DA	109	N9	3.571
C2	DG	110	H2'	2.952
F2	DA	108	C1'	3.236
H6	DC	111	C4	2.966
N9	DA	109	H8	2.896
C23	DA	108	H8	2.972
N1	DG	110	C5	3.601
H3	DG	110	C2'	2.976
C7	DG	112	O6	3.459
C8	DC	111	N4	3.609
H23	DA	108	C2'	2.993
N4	DC	11	H42	2.922
C6	DG	10	C6	3.698
C26	DT	14	N3	3.624
C26	DA	108	C6	3.700
C24	DA	109	N1	3.627
N3	DG	10	N7	3.562
C2	DG	110	N9	3.639
C3	DG	110	C8	3.724
C11	DG	10	C2'	3.726
C5	DG	10	O6	3.509
N3	DG	110	N7	3.587
C24	DA	109	H8	3.040
C28	DA	109	H62	3.040
C11	DG	10	H2"	3.042
C23	DA	109	N9	3.677
C9	DG	110	O6	3.533
C15	DG	10	OP2	3.555
H6	DC	111	H41	2.355
H3	DG	110	H2'	2.355
C7	DG	110	N9	3.689
H28	DG	110	C2	3.067
H4	DG	110	H2"	2.367
H26	DA	108	C6	3.069
H4	DG	112	N7	3.004
H21	DG	110	H8	2.381
N3	DG	110	C5	3.708
C9	DC	11	C5	3.783
C9	DG	10	C2'	3.784
C7	DG	110	C5	3.788
H9	DC	11	N4	3.018

Table S5. Binding interactions of complex **3** with DNA.

Complex 3 interacting atom	Nucleobase	Number of Nucleobase	Type of atom	Bond length (Å)
HC9	DG	110	OP2	1.446
C15	DG	110	OP2	2.344
C15	DA	109	H2"	2.032
HC10	DG	110	H8	1.368
C15	DA	109	C2'	2.913
HC9	DA	109	H2"	1.521
HC9	DG	110	P	2.450
HC9	DA	109	C2'	2.280
O4	DG	110	OP2	2.623
C15	DG	110	H8	2.345
N2	DG	110	N7	2.913
HC10	DG	110	C8	2.405
H52	DG	10	O6	2.260
H42	DG	110	OP2	2.280
H21	DC	111	H42	1.780
C15	DG	110	P	3.389
C1	DG	110	C8	3.255
O5	DG	10	O6	2.847
N2	DC	111	H42	2.506
H21	DC	111	N4	2.521
C1	DG	110	N7	3.297
C15	DG	110	C8	3.389
N2	DG	110	C8	3.336
C7	DG	10	N7	3.352
HC1	DG	12	O6	2.510
N2	DG	110	C5	3.366
HC9	DA	109	C3'	2.748
C3	DG	110	O6	3.240
HC10	DA	109	H2"	2.064
N2	DC	111	N4	3.326
C2	DG	110	N7	3.427
H21	DG	110	N7	2.816
O1	DG	110	C2'	3.373
C2	DG	10	N7	3.522
HC10	DG	110	H2'	2.203
HC1	DG	110	O6	2.688
HC11	DA	109	C2'	2.917
C15	DG	110	O5'	3.427
H21	DG	110	C5	2.928
C3	DC	11	H42	2.938
C15	DA	109	H2'	2.957
C1	DC	111	H42	2.972
O1	DG	110	H2"	2.772
C8	DG	10	N7	3.631
C15	DA	109	C3'	3.717
HC11	DA	109	H2"	2.319
C6	DG	10	C8	3.720
C3	DG	110	C6	3.744
HC9	DG	110	O5'	2.847
C3	DG	12	O6	3.535
C7	DG	10	C8	3.763
C5	DG	10	C8	3.767
C15	DG	110	H2'	3.068
HC	DG	110	C8	3.079
C5	DG	10	H8	3.090
HC1	DG	110	C6	3.090

Table S6. Binding interactions of complex **4** with DNA.

Complex 4 interacting atom	Nucleobase	Number of Nucleobase	Type of atom	Bond length (Å)
HN3	DC	13	N4	2.235
N2	DG	10	OP2	2.813
C5	DG	110	O6	2.878
H9	DC	13	H5	1.785
H5	DG	110	O6	2.270
C6	DG	110	O6	2.972
H9	DC	13	C5	2.542
N3	DC	13	N4	3.105
HN3	DC	13	H42	1.867
N3	DC	13	H42	2.499
H6	DC	13	N4	2.501
H21	DG	10	P	2.811
H6	DG	110	O6	2.487
H5	DG	110	C6	2.714
C9	DC	13	H5	2.744
C2	DG	10	H2'	2.750
N2	DG	10	P	3.550
N2	DG	10	H2'	2.698
H6	DC	13	H41	2.091
N3	DG	12	N7	3.345
C6	DC	13	N4	3.447
C9	DG	12	C8	3.541
HN3	DG	12	N7	2.783
C9	DC	13	C5	3.579
N2	DG	10	O5'	3.328
C5	DG	110	C6	3.603
C9	DG	12	H8	2.908
C2	DG	10	C2'	3.608
C3	DG	10	H8	2.924
HN3	DC	13	C4	2.942
H5	DG	110	C5	2.959
H5	DG	110	N7	2.894
C3	DG	10	C8	3.670
C6	DC	13	H41	2.970
N2	DG	10	C2'	3.596
H3	DG	10	OP2	2.772
H9	DG	12	C8	2.974
C3	DG	10	OP2	3.515
C1	DG	10	C2'	3.778
C7	DG	10	C2'	3.781
H21	DG	10	O5'	2.892

Table S7. Binding interactions of complex **5** with DNA.

Complex 5 interacting atom	Nucleobase	Number of Nucleobase	Type of atom	Bond length (Å)
C2	DG	110	C2	0.530
N1	DG	110	C6	0.659
C25	DA	109	C8	0.769
C24	DA	109	C8	0.817
C1	DG	110	C6	0.919
C8	DG	110	C5	0.977
C24	DA	109	N7	0.933
C7	DG	110	N3	0.937
C27	DA	109	C1'	1.035
N1	DG	110	C5	1.027
C27	DA	109	C2'	1.203
C3	DG	110	N2	1.144
C7	DG	110	C2	1.258
C7	DG	110	C4	1.263
C26	DA	109	C1'	1.322
C2	DG	110	N3	1.271
C23	DA	109	N7	1.280
C26	DA	109	N9	1.280
N2	DG	110	N1	1.211
C6	DC	111	C4	1.372
C8	DG	110	C4	1.422
C3	DG	110	C2	1.457
H5	DC	111	N1	0.691
C2	DG	110	N1	1.427
C27	DA	109	N9	1.433
C6	DG	110	N3	1.438
C5	DC	111	C2	1.552
C8	DG	110	C6	1.572
H6	DC	111	C4	0.889
C1	DG	110	N1	1.542
C26	DA	109	C8	1.619
H27	DA	109	C2'	0.955
N1	DG	110	O6	1.369
C1	DG	110	O6	1.467
C25	DA	109	H8	0.994
C4	DG	110	H22	1.005
N10	DA	109	C8	1.630
C2	DG	110	N2	1.633
C25	DA	109	N9	1.634
F2	DA	108	C1'	1.309
H28	DG	110	C8	1.037
H6	DC	111	C5	1.059
N2	DG	110	C2	1.716
C4	DG	110	N2	1.765
C25	DA	109	N7	1.770
C5	DC	111	N1	1.770
C26	DA	109	C2'	1.847
C5	DC	111	N3	1.781
C6	DC	111	C5	1.867
H27	DA	109	C1'	1.168
C1	DG	110	C5	1.871
C6	DC	111	N3	1.802
N2	DG	110	C6	1.814
H5	DC	111	C2	1.197
C3	DG	110	H22	1.211
H26	DA	109	O4'	1.037
C26	DA	109	O4'	1.741

C3	DG	110	N3	1.872
C7	DG	110	N1	1.882
C28	DA	109	N9	1.884
C7	DG	110	C5	1.967
N3	DG	110	C5	1.915
C28	DG	110	C8	2.005
C28	DG	110	N7	1.939
C24	DA	109	H8	1.320
N10	DG	110	N7	1.888
N4	DG	110	N7	1.893
C5	DG	110	N3	1.970
C2	DG	110	C4	2.050
N10	DA	109	N7	1.905
N1	DG	110	N7	1.932
C28	DA	109	C8	2.100
C6	DG	110	C4	2.102
C8	DG	110	N7	2.029
C24	DA	109	C5	2.108
C27	DA	109	C8	2.126
C5	DC	111	C4	2.135
F2	DA	108	C2'	1.715
C24	DA	109	N9	2.063
C6	DG	110	C2	2.145
N1	DG	110	N1	1.999
C23	DA	109	C8	2.178
C5	DC	111	C6	2.180
F2	DA	108	H1'	1.069
C6	DC	111	N4	2.115
H5	DC	111	C6	1.496
C4	DG	110	N3	2.128
C8	DG	110	N1	2.132
C4	DG	110	C2	2.245
N3	DG	110	C4	2.181
N3	DG	110	N7	2.111
C27	DA	109	H2"	1.578
C7	DG	110	C6	2.282
C8	DG	110	N3	2.215
N3	DC	111	N4	2.144
C28	DA	109	C1'	2.299
H28	DG	110	H8	0.902
C4	DC	111	C2	2.306
N9	DA	109	N7	2.160
H26	DA	109	C1'	1.615
C28	DA	109	C2'	2.328
C27	DA	109	H2'	1.629
N10	DA	109	N9	2.181
H28	DG	110	N7	1.575
C5	DC	111	C5	2.359
N1	DG	110	C4	2.288
C2	DG	110	C6	2.365
H1	DA	109	C6	1.669
H6	DC	111	N4	1.609
HN3	DC	111	H42	0.995
C8	DG	110	C2	2.397
C25	DA	108	H1'	1.699
C26	DA	109	H8	1.713
C27	DA	109	H1'	1.714
C7	DC	111	C4	2.422
N3	DC	111	H42	1.648
F2	DA	109	C8	2.007

N3	DG	110	C8	2.364
C6	DC	111	C2	2.442
C26	DA	109	H2'	1.746
C8	DG	110	N9	2.372
H1	DG	110	O6	1.527
C1	DA	109	C6	2.456
N4	DG	110	C5	2.382
C6	DC	111	C6	2.478
N2	DG	110	H1	1.705
HN3	DC	111	N4	1.706
H1	DA	109	N6	1.715
H26	DA	109	C4'	1.792
H3	DG	110	N2	1.722
C25	DA	108	C1'	2.498
H1	DG	110	C6	1.801
C23	DA	109	C5	2.509
C5	DG	110	C2	2.511
F2	DA	108	N9	2.024
C7	DG	110	N2	2.444
C27	DA	109	O4'	2.326
C7	DC	111	N4	2.458
H27	DA	109	H2"	1.141
C2	DG	110	C5	2.543
N10	DA	109	C5	2.480
N2	DG	110	C5	2.481
C8	DC	111	N4	2.489
C25	DA	109	C1'	2.566
C8	DG	110	C8	2.568
C25	DA	109	C4	2.572
C7	DG	110	N9	2.504
C1	DG	110	C2	2.579
C5	DG	110	N2	2.506
C24	DA	109	C4	2.588
N3	DG	110	N9	2.439
C27	DA	109	C3'	2.590
C25	DA	109	C5	2.592
N4	DG	110	C8	2.520
C26	DA	109	C4	2.606
H27	DA	109	C3'	1.914
C28	DG	110	H8	1.916
N2	DG	110	N3	2.480
C27	DA	109	C4	2.630
C28	DA	109	C4	2.633
H5	DC	111	C1'	1.939
N6	DG	110	O6	2.361
C26	DA	109	C4'	2.659
C5	DC	111	O2	2.446
H21	DG	110	N1	1.895
C3	DG	110	H21	1.984
H23	DA	109	N7	1.922
F2	DA	108	H2"	1.584
C3	DG	110	N1	2.638
N2	DG	110	N2	2.569
N10	DA	109	C4	2.648
C1	DG	110	C4	2.724
H27	DA	109	H1'	1.331
C5	DG	110	H22	2.037
N2	DG	110	C4	2.667
C1	DG	110	H1	2.046
C1	DA	109	N1	2.674

N10	DG	110	C8	2.688
C4	DC	111	O2	2.554
H26	DA	109	O5'	1.874
C4	DC	111	N3	2.701
H5	DC	111	N3	2.003
C6	DC	111	N1	2.710
C28	DA	109	H2"	2.100
N3	DG	110	C6	2.726
C7	DC	111	N3	2.729
N2	DA	109	N1	2.657
H6	DC	111	N3	2.042
C4	DC	111	N1	2.742
H26	DA	109	C2'	2.118
C8	DG	110	O6	2.600
C26	DA	108	H1'	2.127
N10	DA	109	H8	2.057
C26	DA	109	C3'	2.836
C26	DA	109	O5'	2.650
C6	DG	110	N2	2.777
C1	DA	109	N6	2.785
H6	DC	111	C6	2.170
C2	DG	110	H1	2.174
C6	DG	110	N9	2.801
C5	DC	111	C1'	2.885
F2	DA	109	N7	2.391
H5	DC	111	C5	2.201
H26	DA	109	C5'	2.211
H26	DA	109	N9	2.138
H4	DG	110	H22	1.519
C9	DG	110	N7	2.846
N2	DG	110	O6	2.633
C26	DA	109	N7	2.865
C28	DA	109	N7	2.880
C1	DA	109	C5	2.957
N1	DG	110	C2	2.888
C25	DA	108	C2'	2.973
C2	DG	110	H22	2.276
H21	DG	110	C2	2.293
C1	DG	110	N7	2.921
H3	DG	110	C2	2.311
N10	DG	110	C5	2.940
C2	DG	110	H21	2.321
H6	DC	111	H5	1.621
C27	DA	109	H8	2.324
C27	DA	109	C4'	3.029
H1	DA	109	N1	2.259
C25	DA	109	C2'	3.047
C25	DA	108	N9	2.981
H5	DC	111	C4	2.359
N3	DC	111	C4	2.993
N1	DG	110	C8	2.998
H28	DG	110	N9	2.298
C27	DG	110	C8	3.074
C26	DA	109	H1'	2.379
H27	DA	109	N9	2.305
H21	DA	109	N1	2.307
N9	DA	109	C5	3.008
C3	DG	110	C4	3.087
C8	DC	111	C4	3.094
C5	DG	110	C4	3.096

F2	DA	109	H8	1.978
HN3	DC	111	C4	2.401
C25	DA	109	O4'	2.905
H5	DC	111	O2	2.188
C28	DG	110	C5	3.110
C28	DA	109	C5	3.112
H23	DA	108	C8	2.412
C7	DC	111	C5	3.116
C6	DG	110	C1'	3.118
N9	DG	110	O6	2.829
C9	DG	110	C8	3.126
H15	DG	12	O6	2.206
C28	DA	109	H8	2.435
N4	DG	110	C6	3.064
N2	DA	109	C6	3.064
C6	DG	110	C5	3.142
C28	DA	109	H2'	2.444
H1	DA	109	C5	2.448
N2	DA	109	C2	3.076
C23	DA	109	H8	2.453
H6	DG	110	N3	2.388
C15	DG	12	O6	2.944
H3	DG	110	H22	1.765
H26	DA	109	C3'	2.470
C25	DA	108	H2"	2.478
N9	DA	109	C8	3.103
F2	DA	108	C8	2.764
C6	DG	110	H1'	2.488
C26	DA	108	C1'	3.188
C1	DG	110	N3	3.114
H27	DA	109	O3'	2.293
C6	DG	110	N1	3.123
C15	DG	110	O6	2.981
C26	DA	109	C5'	3.203
C22	DG	110	O6	2.987
C8	DC	111	H42	2.515
H27	DA	109	O4'	2.315
H1	DG	110	N1	2.443
N1	DG	110	N3	3.084
C24	DG	110	N7	3.167
C23	DA	108	C8	3.243
N3	DG	110	N3	3.094
C28	DG	110	N9	3.182
N4	DG	110	C4	3.182
C7	DG	110	N7	3.185
HN3	DG	110	C4	2.560
N10	DA	109	C1'	3.186
C26	DA	109	C5	3.263
H71	DC	11	H5	1.868
F2	DA	109	N9	2.775
H21	DG	110	C6	2.571
H4	DG	110	N2	2.498
C1	DA	109	C2	3.275
F2	DA	108	O4'	2.656
C6	DC	111	H5	2.577
H4	DC	111	C2	2.578
H6	DG	110	C4	2.581
C24	DA	109	C1'	3.291
C25	DA	109	H2'	2.594
H21	DT	14	N3	2.522

HN3	DC	111	C5	2.597
H26	DA	109	C8	2.598
C8	DC	111	H41	2.617
C5	DC	111	N4	3.244
C25	DA	109	O5'	3.130
N3	DC	111	H41	2.557
H6	DC	111	H42	1.936
C28	DA	109	H1'	2.636
H4	DC	111	O2	2.417
C7	DG	110	C8	3.337
N7	DG	12	N7	3.188
C23	DA	109	C6	3.340
N2	DC	13	N3	3.193
C27	DG	110	N7	3.269
H27	DA	109	C4'	2.644
Ni1	DG	110	N7	2.062
C4	DC	111	C4	3.353
N6	DG	110	C6	3.279
N9	DA	109	H62	2.580
HN3	DG	110	N9	2.581
N7	DC	11	H5	2.581
C27	DA	109	N7	3.282
N1	DG	110	N9	3.210
C5	DC	111	O4'	3.164
C7	DC	111	H41	2.664
H27	DA	109	H2'	1.964
C6	DC	111	H41	2.667
C4	DC	111	C1'	3.367
C6	DC	111	H42	2.672
C4	DG	110	H21	2.676
H15	DC	11	H42	1.980
C24	DA	109	C6	3.384
H21	DG	110	H1	1.986
C7	DG	110	C1'	3.389
N4	DG	110	N9	3.239
F2	DA	108	C3'	2.970
N1	DA	109	C6	3.315
N1	DA	109	C5	3.315
C26	DA	109	H2"	2.701
N4	DC	111	H42	2.638
H71	DG	12	N7	2.640
C3	DC	111	C2	3.418
N7	DG	10	H2"	2.644
C27	DG	110	H8	2.720
N8	DA	109	H62	2.650
H5	DC	111	O4'	2.525
N10	DA	109	C2'	3.351
C2	DG	110	N9	3.353
H26	DA	108	H1'	2.035
C4	DC	111	C6	3.437
N9	DA	109	N6	3.289
C25	DA	109	OP2	3.242
C23	DA	109	H62	2.744
H1	DG	110	C5	2.746
C1	DC	13	H41	2.747
N4	DC	111	N4	3.298
H28	DG	110	C5	2.749
C3	DC	111	N3	3.380
HN3	DG	110	C5	2.756
C5	DG	110	H1'	2.757

H23	DA	109	C8	2.761
C4	DG	110	C4	3.465
C23	DA	109	N6	3.390
C2	DC	111	N3	3.392
C23	DA	109	N9	3.393
H21	DT	14	H3	2.070
C27	DA	109	N3	3.401
C27	DA	109	C5	3.479
N1	DG	110	H1	2.708
C26	DA	109	P	3.655
N3	DC	111	C5	3.410
N8	DA	109	N7	3.335
H6	DC	111	C2	2.795
F2	DA	108	C4	3.078
HN3	DG	110	C8	2.799
C6	DG	110	H22	2.800
H3	DG	110	H21	2.100
F2	DA	108	H2'	2.385
C27	DA	109	O3'	3.306
C7	DG	110	H1	2.807
C11	DG	10	N7	3.436
C1	DA	109	C4	3.512
H28	DA	109	C2'	2.813
C1	DC	13	N3	3.446
H1	DA	109	H61	2.122
H71	DG	10	H2"	2.124
H23	DA	108	H8	2.133
N3	DG	110	N1	3.385
N2	DT	14	N3	3.388
H21	DG	110	N2	2.763
C7	DC	111	C2	3.538
C23	DA	109	C4	3.540
H26	DA	109	H2'	2.141
C2	DC	111	C4	3.551
N8	DG	110	O6	3.257
H28	DA	109	H2"	2.156
C24	DA	108	C1'	3.558
N7	DG	10	C2'	3.484
N5	DG	110	N7	3.419
F2	DA	109	O5'	2.949
H21	DA	109	C2	2.875
N9	DA	109	C6	3.501
C4	DC	111	O4'	3.386
C28	DA	109	N3	3.514
N2	DG	110	H21	2.814
H28	DA	109	N9	2.817
C26	DA	109	OP2	3.393
C9	DG	110	C5	3.595
H71	DC	11	C5	2.899
H6	DC	111	N1	2.830
C7	DG	110	H22	2.906
C7	DC	111	H42	2.907
N3	DG	110	C2	3.533
H27	DG	110	P	3.082
H1	DA	109	H62	2.213
C23	DA	108	N9	3.539
C25	DA	109	P	3.785
C22	DC	13	N4	3.550
C6	DG	110	C6	3.627
C3	DC	13	O2	3.407

HN3	DC	111	H5	2.234
N2	DT	14	H3	2.863
C10	DG	110	N7	3.566
H4	DC	111	N1	2.868
C24	DA	109	C2'	3.643
N3	DG	110	C1'	3.569
C26	DA	109	N3	3.570
F2	DA	109	C5	3.226
H3	DG	110	N3	2.872
F2	DA	108	C4'	3.228
C8	DG	12	O6	3.429
N2	DA	109	N6	3.504
C8	DG	110	C1'	3.657
C24	DA	108	N9	3.586
H6	DG	110	N9	2.887
N4	DG	110	O6	3.368
H28	DA	109	C1'	2.963
C24	DA	108	H1'	2.965
C25	DA	108	C4	3.667
C25	DA	108	C8	3.671
N10	DG	110	H8	2.898
C5	DG	110	C1'	3.676
C4	DG	110	N1	3.602
H21	DA	109	C6	2.979
N10	DG	110	C6	3.605
C15	DC	11	H5	2.999
C1	DC	13	N4	3.625
C21	DC	13	N4	3.628
C22	DC	13	H41	3.003
C7	DG	110	O6	3.484
C2	DG	110	O6	3.484
H4	DC	111	C1'	3.006
C6	DC	111	O2	3.486
C15	DG	110	C6	3.708
N8	DA	109	N6	3.560
H15	DC	11	N4	2.935
N6	DC	13	H41	2.937
F2	DA	109	P	3.463
N7	DC	11	C5	3.640
HN3	DG	110	N7	2.940
C28	DG	110	C4	3.716
N10	DA	109	C6	3.643
C4	DC	111	C5	3.721
C15	DC	11	H42	3.023
C1	DG	110	N2	3.653
Ni1	DG	110	O6	2.301
N7	DG	12	O6	3.438
H26	DA	109	P	3.209
C9	DC	111	H42	3.039
H3	DT	14	O2	2.820
C8	DG	110	H1	3.041
C8	DC	111	C5	3.744
N9	DG	110	N7	3.597
H1	DC	13	H41	2.349
C8	DG	110	N2	3.675
C17	DG	10	C2'	3.751
H23	DA	108	N9	2.977
C6	DG	12	H1	3.052
C3	DG	110	C6	3.752
H23	DA	109	C5	3.053

C3	DG	110	H1	3.059
C16	DC	13	N4	3.686
H26	DA	108	C1'	3.066
H5	DG	110	N3	2.993
Ni1	DG	110	C5	2.559
N3	DG	110	O6	3.475
N9	DG	110	C6	3.697
H6	DG	110	C1'	3.079
H28	DG	110	C4	3.082
H5	DC	111	H6	2.384
F2	DA	109	OP2	3.171
C2	DC	111	N4	3.716
H21	DT	14	C2	3.092
C15	DC	13	N4	3.719
N1	DA	109	N6	3.645
C1	DA	109	H61	3.099

Table S8. Binding interactions of complex **6** with DNA.

Complex 6 interacting atom	Nucleobase	Number of Nucleobase	Type of atom	Bond length (Å)
HC5	DG	12	H8	1.799
HC9	DG	10	H3'	1.836
C15	DG	10	H3'	2.539
HC5	DG	12	C8	2.564
N2	DG	10	OP2	3.030
F1	DG	12	H2'	2.236
HN	DG	12	N7	2.604
H11	DG	10	H3'	1.988
O1	DC	11	OP2	3.091
O1	DG	10	H3'	2.595
H11	DC	11	OP2	2.604
HC9	DG	10	C3'	2.809
HC3	DC	11	H42	2.118
C9	DG	12	H8	2.833
C7	DG	10	C2'	3.578
C5	DG	110	O6	3.375
C9	DG	12	C8	3.604
C5	DC	11	H42	2.907
C15	DG	10	C3'	3.613
F1	DG	12	C2'	3.195
C8	DG	10	C2'	3.628
C9	DC	11	OP2	3.433
HC5	DG	12	N7	2.863
H11	DG	10	C3'	2.939
C7	DG	10	H2'	2.949
HC9	DG	10	C5'	2.952
C6	DC	11	H5	2.968
C1	DG	10	OP2	3.496
C6	DG	10	C2'	3.697
H21	DG	10	OP2	2.797
N3	DG	12	N7	3.550
N3	DG	10	H2"	2.934
HC3	DG	12	O6	2.790
HC4	DC	11	H5	2.313
HC9	DG	10	H5"	2.316
C10	DC	11	OP2	3.538
C5	DG	12	O6	3.522
F1	DG	12	H8	2.626
HC4	DG	12	O6	2.836
C6	DG	12	O6	3.544
H11	DC	11	P	3.238
N3	DG	10	C2'	3.695
C6	DG	10	H2"	3.089
C5	DG	10	C8	3.789
C4	DG	10	C8	3.796
C15	DG	10	OP1	3.598

Table S9. Binding interactions of complex **1** with BSA.

Complex 1 interacting atom	Amino acid residue	Number of amino acid	Type of atom	Bond length (Å)
H3	PHE	205	CD1	2.264
H3	PHE	205	HD1	1.578
Br1	ASP	323	CG	3.700
Br1	ARG	208	HB2	3.103
C3	PHE	205	CD1	3.162
Br1	ASP	323	OD2	3.688
Br1	ARG	208	HD2	3.213
C4	LEU	480	H	2.509
Br1	ARG	208	CD	3.954
H4	SER	479	HA	1.841
C5	LYS	350	HZ2	2.603
N1	ARG	208	HE	2.528
H5	SER	479	OG	2.415
C6	LYS	350	HD2	2.633
C3	PHE	205	HD1	2.635
Br1	ARG	208	CZ	4.055
H5	SER	479	HG	1.936
Br1	ARG	208	NE	3.994
Br1	ARG	208	CB	4.076
Br1	ARG	208	NH1	4.005
H1	ARG	208	CG	2.670
C5	LYS	350	HD2	2.686
H4	SER	479	CA	2.706
H12	LEU	326	O	2.489
C11	LEU	330	HD23	2.717
H12	LEU	326	C	2.720
C1	ARG	208	HE	2.723
Br1	ASP	323	OD1	3.925
N5	ALA	212	HB2	2.651
H6	LYS	350	HD2	2.037
N2	ALA	209	HB3	2.681
C12	LEU	326	HB2	2.761
C5	SER	479	OG	3.279
H1	ARG	208	HG2	2.096
H4	LEU	480	H	2.099
C10	ALA	212	CB	3.513
C12	LEU	326	C	3.519
C1	ALA	209	HB3	2.821
Br1	ASP	323	CB	4.246
C10	ALA	212	HB2	2.846
H5	LYS	350	HD2	2.152
C4	LEU	480	N	3.486
C1	ARG	208	HG2	2.866
C5	LYS	350	NZ	3.503
H11	LEU	330	HD23	2.189
C5	LEU	480	H	2.892
Br1	ARG	208	CG	4.326
C4	SER	479	HA	2.916
C5	LYS	350	CD	3.616
C1	ARG	208	CG	3.622
C11	LEU	330	CD2	3.622
C6	LYS	350	CD	3.639
N1	ARG	208	NE	3.502
C5	SER	479	HG	2.959
C1	ALA	209	CB	3.667
H5	LYS	350	CD	2.978
C12	LEU	326	CB	3.685

C13	GLY	327	N	3.618
N5	ALA	212	CB	3.621
H11	ALA	349	CB	3.002
H4	LEU	480	N	2.929
C12	LEU	326	O	3.487
C12	GLY	327	N	3.634
H13	GLY	327	N	2.937
C4	SER	479	CA	3.721
C9	ALA	212	CB	3.722
H5	LYS	350	CE	3.025
C5	LYS	350	CE	3.727
C1	ALA	209	CA	3.727
C4	PHE	205	CD1	3.734
H6	LYS	350	CD	3.035
N2	ALA	209	CB	3.662
H12	GLY	327	N	2.964
Br1	ARG	208	O	4.243
H4	SER	479	CB	3.045
H3	PHE	205	CE1	3.047
C1	ARG	208	NE	3.676
N1	ARG	208	HG2	2.988
C3	PHE	205	CE1	3.765
H12	GLY	327	HA2	2.368
N2	PHE	205	HB3	3.002
H5	VAL	481	HG23	2.382
C4	SER	479	OG	3.586
H1	ARG	208	HE	2.392
C12	GLY	327	HA2	3.094

Table S10. Binding interactions of complex **2** with BSA.

Complex 2 interacting atom	Amino acid residue	Number of amino acid	Type of atom	Bond length (Å)
H12	PRO	110	HG2	1.197
C12	PRO	110	HG2	2.202
H12	PRO	110	CG	2.275
C27	LEU	189	HD21	2.453
H23	LYS	114	CB	2.510
C12	PRO	110	CG	3.238
C28	LEU	189	HD21	2.553
C6	LEU	189	HD12	2.571
C27	ARG	185	HH21	2.607
H8	LYS	114	HB2	1.944
H23	LYS	114	HB2	1.948
H27	LEU	189	HD21	1.948
H23	LYS	114	CG	2.676
F1	PRO	110	HD2	2.260
C7	LEU	189	HD12	2.682
C26	ARG	185	HH21	2.692
C12	ARG	144	HG2	2.697
C5	LEU	189	HD12	2.733
H13	LEU	112	O	2.516
C13	LEU	112	H	2.736
H27	LEU	189	CD2	2.748
H13	LEU	112	N	2.678
C27	LEU	189	CD2	3.454
F2	LYS	114	HG3	2.344
F2	LEU	115	H	2.369
H13	LEU	112	H	2.116
H28	LEU	189	HD21	2.137
F1	ARG	144	O	2.898
C13	LEU	112	N	3.469
C28	ARG	185	HH21	2.853
C13	LEU	112	O	3.334
N8	LYS	114	HB2	2.783
C23	LYS	114	CB	3.563
C23	LYS	114	HB2	2.866
F1	PRO	110	CD	3.161
H23	LYS	114	CA	2.888
C28	LEU	189	CD2	3.591
C2	LEU	189	HD12	2.896
C27	ARG	185	NH2	3.527
C7	LEU	189	CD1	3.608
C13	ARG	144	HG2	2.923
C2	LEU	189	CD1	3.636
C11	PRO	110	HG2	2.939
C6	LEU	189	CD1	3.654
H13	LEU	112	C	2.954
H13	LEU	112	HB3	2.262
C4	LEU	189	HD12	2.969
C23	LYS	114	CG	3.684
C25	ARG	185	HH21	2.996
H13	LEU	112	CA	2.999
C26	ARG	185	HE	2.999
H23	LYS	114	HG3	2.302
H23	LYS	114	HA	2.314
H28	LEU	189	CD2	3.017
C11	PRO	110	HD2	3.030
C12	ARG	144	CG	3.730
H8	LYS	114	CB	3.032

C12	LEU	112	H	3.038
C26	ARG	185	NH2	3.669
H13	LEU	112	CB	3.046
C12	PRO	110	CD	3.748
C11	PRO	110	CG	3.752
C3	LEU	189	HD12	3.061
C5	LEU	189	CD1	3.763
C3	LEU	189	CD1	3.766
H12	PRO	110	CD	3.076
H23	LYS	114	CD	3.077
C28	ARG	185	NH2	3.703
F1	PRO	110	CG	3.362
C23	LYS	114	HD2	3.091

Table S11. Binding interactions of complex **3** with BSA.

Complex 3 interacting atom	Amino acid residue	Number of amino acid	Type of atom	Bond length (Å)
HC6	LEU	112	O	1.994
H53	GLU	424	OE1	2.024
HN	ARG	144	O	2.145
O5	ARG	458	NH2	2.799
HC2	ARG	196	HD3	1.727
HC9	LEU	189	HD21	1.759
O5	GLU	424	OE1	2.743
HC2	ARG	196	CD	2.467
N3	ARG	144	O	2.897
H53	GLU	424	CD	2.497
C12	LEU	112	O	3.055
O5	ARG	458	HH21	2.383
HC2	ARG	196	CG	2.616
C5	PRO	146	HD3	2.646
HC3	PRO	146	HD3	1.952
C2	ARG	458	NH1	3.305
O5	GLU	424	CD	3.186
HC9	LEU	189	CD2	2.693
C15	LEU	189	HD21	2.693
C7	ARG	458	NH1	3.353
F1	LEU	112	H	2.318
H42	HIS	145	HE1	2.039
C4	ARG	196	HD3	2.771
C3	SER	192	HG	2.776
H52	ARG	458	NH2	2.703
HC4	ARG	144	O	2.576
C6	PRO	146	HD3	2.800
C6	HIS	145	HA	2.803
C4	ARG	196	CD	3.507
C3	SER	192	OG	3.314
C7	HIS	145	HD1	2.824
C4	ARG	196	CG	3.530
C15	LEU	189	CD2	3.560
N2	ARG	458	HD3	2.816
C7	HIS	145	ND1	3.530
C4	ARG	196	HG2	2.924
HC2	ARG	196	CB	2.942
HC2	ARG	196	HG2	2.254
F1	PRO	110	HG3	2.534
HC3	PRO	146	CD	2.963
C6	ARG	144	O	3.448
H42	HIS	145	CE1	2.978
O5	GLU	424	OE2	3.272
F1	LEU	112	N	3.198
C8	HIS	145	ND1	3.622
C5	ASP	108	OD1	3.480
O4	HIS	145	HE1	2.806
C2	SER	192	OG	3.506
C2	ARG	458	HH11	3.008
HC4	PRO	146	HD3	2.315
HC2	ARG	196	HB2	2.322
H52	ARG	458	HH21	2.323
C2	SER	192	HG	3.031
C5	PRO	146	CD	3.731
C8	ARG	458	NH1	3.667
HC4	HIS	145	HA	2.343
N2	ARG	458	NH1	3.595

O4	LEU	189	CD2	3.546
H42	LEU	189	CD2	3.058
H53	GLU	424	OE2	2.843
C2	HIS	145	HD1	3.081
C4	ARG	196	HB2	3.088
HC3	ASP	108	OD1	2.874
HC5	PRO	110	CG	3.097
C4	ARG	196	CB	3.799

Table S12. Binding interactions of complex **4** with BSA.

Complex 4 interacting atom	Amino acid residue	Number of amino acid	Type of atom	Bond length (Å)
H5	PRO	146	HD3	1.371
C5	PRO	146	HD3	2.178
H5	PRO	146	CD	2.325
Cl1	LEU	189	HB3	2.525
C5	HIS	145	HA	2.472
Cl1	LEU	189	CB	3.330
H3	ARG	196	HB2	1.828
C5	PRO	146	CD	3.243
N2	SER	192	HG	2.469
H3	ARG	196	HD2	1.897
C2	SER	192	OG	3.103
C4	PRO	146	HD3	2.605
N1	ARG	458	HD3	2.538
Cl1	LEU	189	HD22	2.739
H3	ARG	196	CB	2.630
C2	SER	192	HG	2.631
C3	ARG	196	HD2	2.673
H3	ARG	196	CD	2.674
H3	ARG	196	CG	2.675
C7	ARG	458	NH1	3.305
C8	ARG	458	NH1	3.306
H5	HIS	145	HA	2.035
Cl1	LEU	189	O	3.354
C1	ARG	458	HD3	2.766
C3	ARG	196	CD	3.483
Cl1	LEU	189	HD12	2.911
Cl1	LEU	189	CA	3.625
C10	GLU	424	OE2	3.295
C5	HIS	145	CA	3.518
C3	ARG	196	CG	3.520
Cl1	LEU	189	CD2	3.635
C3	ARG	196	HB2	2.837
C3	SER	192	OG	3.338
N2	SER	192	OG	3.274
N2	ALA	193	HA	2.790
N5	GLU	424	OE2	3.273
C7	HIS	145	HD1	2.886
N3	ARG	458	CZ	3.520
C1	ALA	193	HA	2.899
Cl1	LEU	189	CG	3.721
C1	SER	192	HG	2.913
H4	TYR	147	HD2	2.214
N1	ARG	458	CD	3.551
C3	ARG	196	CB	3.634
Cl1	LEU	189	C	3.751
C8	ARG	458	CZ	3.652
C6	ARG	458	NH1	3.578
Cl1	LEU	189	CD1	3.766
C4	PRO	146	CD	3.662
N3	ARG	458	NH1	3.528
Cl2	ARG	458	HD3	3.089
C6	HIS	145	HD1	2.981
H21	ALA	193	HA	2.282
C10	GLU	424	CD	3.682
C12	GLU	424	HG3	2.996
C4	ASP	108	OD1	3.480
C6	HIS	145	ND1	3.631

C13	SER	428	OG	3.514
C3	ARG	196	HG2	3.014
H21	ARG	196	CB	3.017
C4	ARG	196	HD2	3.020
H4	PRO	146	HD3	2.331
H13	SER	428	OG	2.833
C12	GLU	424	CG	3.734
Cl2	ARG	458	CG	3.844
C1	ALA	193	CA	3.755
C5	ARG	144	O	3.547
C6	ARG	144	O	3.550
C1	ARG	458	CD	3.771
C7	SER	192	OG	3.574
Cl2	ARG	458	CB	3.891
C14	SER	428	OG	3.589
Cl2	ARG	458	HB2	3.205

Table S13. Binding interactions of complex **5** with BSA.

Complex 5 interacting atom	Amino acid residue	Number of amino acid	Type of atom	Bond length (Å)
H23	LYS	114	HB3	1.679
H19	LEU	115	HG	1.699
H19	LEU	115	CG	2.432
H19	LEU	115	CB	2.503
H19	LEU	115	HB2	1.850
H13	LEU	112	H	1.868
C19	LEU	115	HG	2.598
H20	LEU	115	H	1.914
H13	LEU	112	N	2.580
C20	LEU	115	H	2.656
H12	PRO	110	CD	2.660
H20	LYS	114	HA	1.961
C5	SER	428	OG	3.181
C23	LYS	114	HB3	2.713
H12	ASP	111	H	2.017
H17	ILE	141	CD1	2.741
H5	SER	428	OG	2.542
H23	LYS	114	CB	2.750
C19	LEU	115	CG	3.465
C16	ARG	144	HD2	2.766
H12	ASP	111	N	2.694
N2	ARG	185	HH22	2.696
C19	LEU	115	HB2	2.787
N7	LEU	189	HD21	2.717
H71	HIS	145	NE2	2.719
H8	LYS	114	HA	2.103
C1	ARG	185	HH22	2.817
C17	ILE	141	CD1	3.530
C12	ASP	111	N	3.461
C13	LEU	112	H	2.837
C12	ASP	111	H	2.840
H12	PRO	110	HD2	2.140
N7	HIS	145	NE2	3.393
H12	PRO	110	CG	2.851
C19	LEU	115	CB	3.552
C21	ARG	144	HD2	2.858
H12	PRO	110	N	2.790
C15	LEU	189	HD21	2.868
C12	PRO	110	HD2	2.869
C1	ARG	185	NH2	3.497
H20	LEU	115	N	2.798
H8	LYS	114	CB	2.874
C12	PRO	110	HG3	2.875
C12	PRO	110	CD	3.582
F1	SER	109	HA	2.472
C19	LEU	115	H	2.894
H8	LYS	114	CA	2.903
H12	PRO	110	HG3	2.205
H20	LYS	114	CA	2.935
C13	LEU	112	N	3.584
C2	LEU	189	CD1	3.661
N7	LEU	189	CD2	3.591
C18	ILE	141	CD1	3.667
C20	LEU	115	N	3.595
C17	ARG	144	CD	3.673
F2	GLU	519	OE1	3.035
H18	ILE	141	HD12	2.285

C4	SER	428	OG	3.487
C12	PRO	110	CG	3.688
H17	ILE	141	HD13	2.288
C18	ARG	144	CD	3.690
C18	ILE	141	HD12	2.998
C20	LYS	114	HA	3.012
C16	ARG	144	CD	3.717
H18	ILE	141	CD1	3.029
C17	ARG	144	HD2	3.030
H8	LYS	114	CG	3.033
F1	ARG	458	HH22	2.621
F1	ARG	458	NH2	3.254
C23	LYS	114	CB	3.752
H26	ILE	522	HD12	2.354
C19	ARG	144	CD	3.755
C19	ARG	144	NE	3.686
C7	LEU	189	HD13	3.063
C20	ARG	144	NE	3.688
H71	LEU	189	CD2	3.065
N2	ARG	185	NH2	3.618
H71	LEU	189	HD21	2.377
N8	LYS	114	HA	3.013
C20	ARG	144	CD	3.797
C15	LEU	189	CD2	3.798
C19	LEU	115	N	3.724

Table S14. Binding interactions of complex **6** with BSA.

Complex 6 interacting atom	Amino acid residue	Number of amino acid	Type of atom	Bond length (Å)
HC2	ALA	212	HB2	1.759
HC1	ARG	208	HB2	1.781
C9	ALA	324	HA	2.668
HC1	ARG	208	CB	2.669
N2	ASP	323	OD2	3.107
HC9	ALA	324	HB3	2.020
C4	ALA	212	HB2	2.737
C15	ALA	324	HB3	2.739
C3	ARG	208	HB2	2.747
C10	THR	231	HG21	2.780
HC2	ALA	212	CB	2.786
F1	PHE	227	CE2	3.083
F1	PHE	227	HE2	2.384
N1	ASP	323	HB3	2.748
HC4	GLY	327	CA	2.835
HC4	GLY	327	HA3	2.162
C1	ASP	323	HB3	2.868
C8	ASP	323	HB3	2.881
O1	ALA	324	N	3.319
C11	THR	231	HG21	2.901
H11	ASP	323	CB	2.905
C1	ASP	323	OD2	3.406
HC9	ALA	324	CB	2.945
N2	LYS	211	HD3	2.881
C6	GLY	327	CA	3.671
C3	ARG	208	O	3.451
C4	ALA	212	CB	3.671
C9	ALA	324	CA	3.680
H21	ARG	208	HB2	2.298
C3	ARG	208	CB	3.700
C10	THR	231	CG2	3.735
C9	THR	231	CG2	3.744
C15	ALA	324	CB	3.744
N3	ASP	323	O	3.461
N2	ARG	208	HB2	2.991
HC1	ARG	208	CA	3.074
C1	ASP	323	CB	3.779
C4	ARG	208	O	3.564
C9	THR	231	HG21	3.091
HC1	ARG	208	O	2.879