Electronic Supplementary Information (ESI)

Synthesis, structures and biomolecular interactions of new silver(I) 5,5-diethylbarbiturate complexes of monophosphines targeting Gram-positive bacteria and breast cancer cells

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Table S1 Crystallographic data and structure refinement for complexes **1**–**4**.

	1	**2**	**3**	**4·0.5MeCN**
empirical formula	$C_{52}H_{52}Ag_2N_4O_6P_2$	$C_{26}H_{32}AgN_2O_3P$	$C_{26}H_{37}AgN_2O_3P$	$C_{27}H_{45.5}AgN_{2.5}O_3P$
formula weight	1106.66	559.38	564.42	571.47
crystal system	monoclinic	triclinic	triclinic	triclinic
space group	$P2/c$	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a, Å	25.3536(9)	9.3467(5)	10.6971(5)	10.8443(6)
b, Å	12.5349(3)	11.5535(6)	11.8519(5)	11.5236(6)
c, Å	21.7484(7)	12.6357(6)	12.6449(6)	13.6228(7)
α, deg	90.00	94.402(4)	63.398(3)	97.443(4)
β, deg	133.372(2)	92.711(4)	73.689(4)	90.550(4)
γ, deg	90.00	105.575(4)	89.817(4)	116.452(4)
V, Å^3	5024.2(3)	1307.23(12)	1361.63(11)	1506.96(15)
T, K	296	296	296	296
Z	4	2	2	2
ρ_{calc} (g cm^{-3})	1.463	1.421	1.377	1.259
μ (mm^{-1})	0.895	0.861	0.827	0.748
F(000)	2256	576	586	600
θ (°)	1.89-26.50	2.27-26.50	1.90-27.59	2.50-26.00
collected reflections	37375	20694	19577	17125
data/restrain/parameters	5215/0/299	5389/0/298	6246/284	5873/298
goodness-of-fit	1.077	1.025	1.057	1.026
R_1 [$I>2\sigma$]	0.0260	0.0235	0.043	0.0423
wR_2	0.0624	0.0620	0.1124	0.1030

Table S2 Temperature-dependent fluorescence emission titration data for the interaction of **1**–**4** with FS-DNA.

EB-exchange						
Complexes	T(K)	K_{SV}(M^{-1}) x 10^{-4}	K_F(M^{-1}) x 10^{-4}	ΔG° (kJ/mol)	ΔH° (kJ/mol)	ΔS° (J/Kxmol)
1	293	2.3	12.2	–28.6	–85.6	–194.4
	297	2.1	8.0	–27.8		
	300	2.0	5.4	–27.3		
2	293	1.5	13.2	–28.7	–91.9	–215.4
	297	1.4	8.1	–27.9		
	300	1.2	5.3	–27.2		
3	293	1.3	14.7	–29.0	–78.5	–168.8
	297	1.1	9.4	–28.3		
	300	1.0	7.0	–27.8		
4	293	1.2	19.7	–29.7	–65.9	–123.5
	297	1.1	13.5	–29.2		
	300	1.0	10.5	–28.8		

Table S3 Temperature-dependent fluorescence emission titration data for the interaction of **1**–**4** with BSA.

Complexes	T(K)	K_{SV}(M^{-1}) x 10^{-5}	K_F(M^{-1}) x 10^{-6}	ΔG° (kJ/mol)	ΔH° (kJ/mol)	ΔS° (J/Kxmol)
1	293	1.1	0.9	–33.5	+16.9	+171.9
	297	0.9	1.0	–34.1		
	300	0.7	1.1	–34.6		
2	293	11.6	1.1	–33.9	+25.5	+202.7
	297	10.8	1.3	–34.7		
	300	10.1	1.4	–35.3		
3	293	12.4	1.2	–34.1	+23.6	+196.9
	297	11.8	1.4	–34.9		
	300	11.0	1.5	–35.5		
4	293	14.6	1.3	–34.3	+33.5	+231.3
	297	14.0	1.5	–35.2		
	300	13.2	1.8	–35.9		

Table S4 Hydrogen bonding and van der Waals interactions and the binding free energy of the most stable docking conformations for complexes **1**–**4** docked into DNA.

Complex	Hydrogen bonding	Distance (Å)	ΔG (kJ mol^{-1})
1	N2-H2A (barb)··· O6(DG16)	1.94	−27.94
	DC9:N4 ··· O1(barb)	2.89	
	N2-H2A (barb)··· O4(DT8)	2.98	
2	N2-H2A (barb)··· O2'(DC3)	2.45	−29.29
	N2-H2A (barb) ··· O4'(DG4)	2.65	
3	N2–H2 (barb)··· O2 (DC3)	2.07	−29.71
	DG22:N2··· O1 (barb)	2.89	
4	N2–H2 (barb)··· O2 (DC3)	2.23	−30.12
	N2-H2(barb)··· O4 '(DG4)	2.89	

Table S5 Hydrogen bonding, binding sites and the binding free energy of the most stable docking conformations for complexes **1**–**4** docked into HSA.

Complex	Hydrogen bonding	Distance (Å)	Hydrophobic interaction	Distance (Å)	Binding free energy ($kJmol^{-1}$)
1	-	-	Alkyl··· LYS190-alkyl	3.58	-32.22
			π···ARG145alkyl	3.97	
2	ARG222:NH_2··· O1-barb	2.83	C15-H15 ··· TRP214π	3.73	-33.89
			C24··· LEU238alkyl	3.95	
			C26··· ILE290alkyl	4.01	
3	N2-H2 (barb) ··· ASP451:OD2	2.74	LYS199:CB ···π	3.91	-34.31
			TRP214π ···π	3.96	
			ALA215- alkyl ··· alkyl	3.99	
4	LYS195:NZ··· O1-barb	2.81	C10-H10 ··· TRP214π	3.88	-35.16
	ARG222:NH_2··· O3-barb	2.81			
	ARG218:NE··· O3-barb	2.85			
	N2-H2 (barb) ··· ASP451:OD1	2.92			

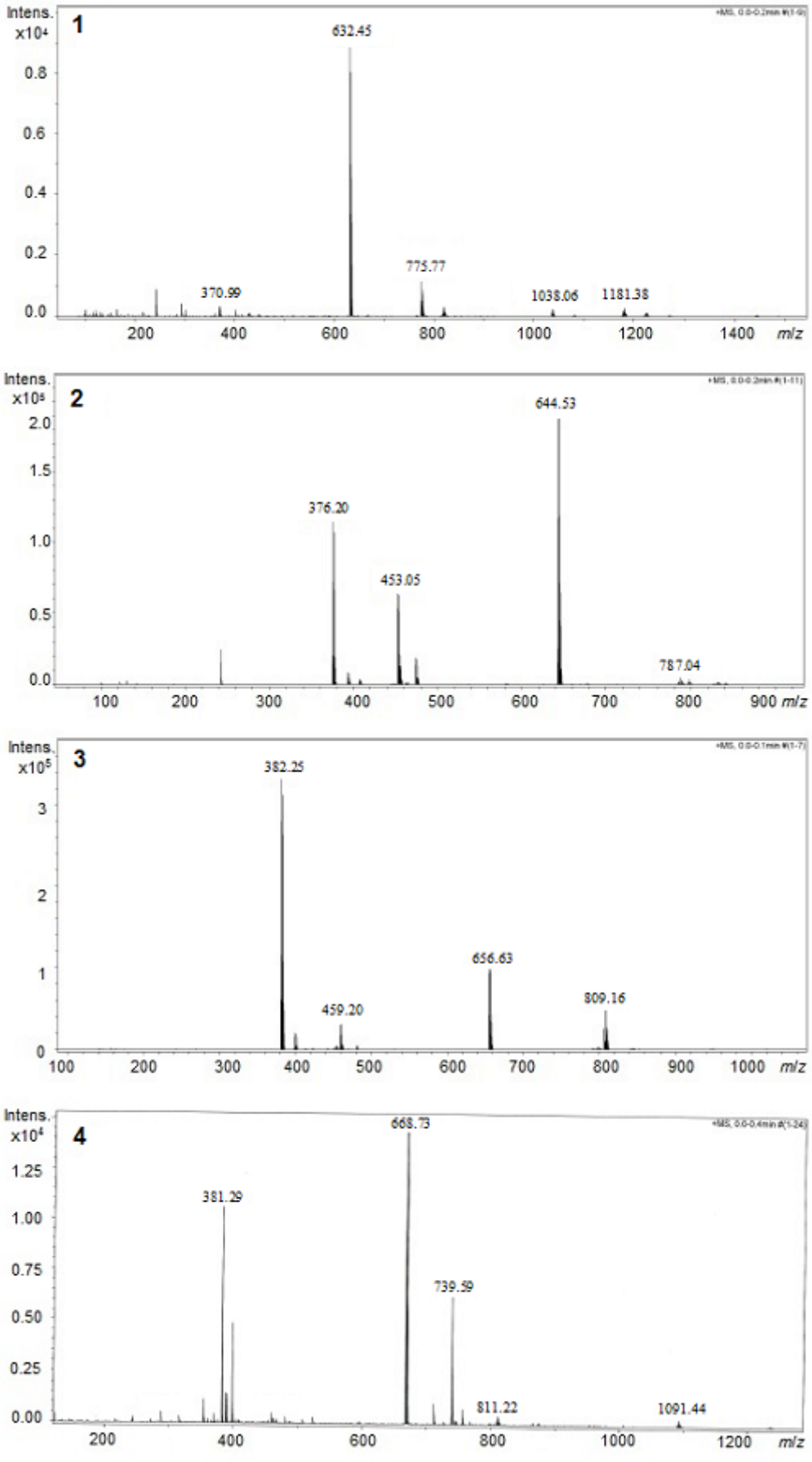


Fig. S1 ESI-MS spectra of **1**–**4**.

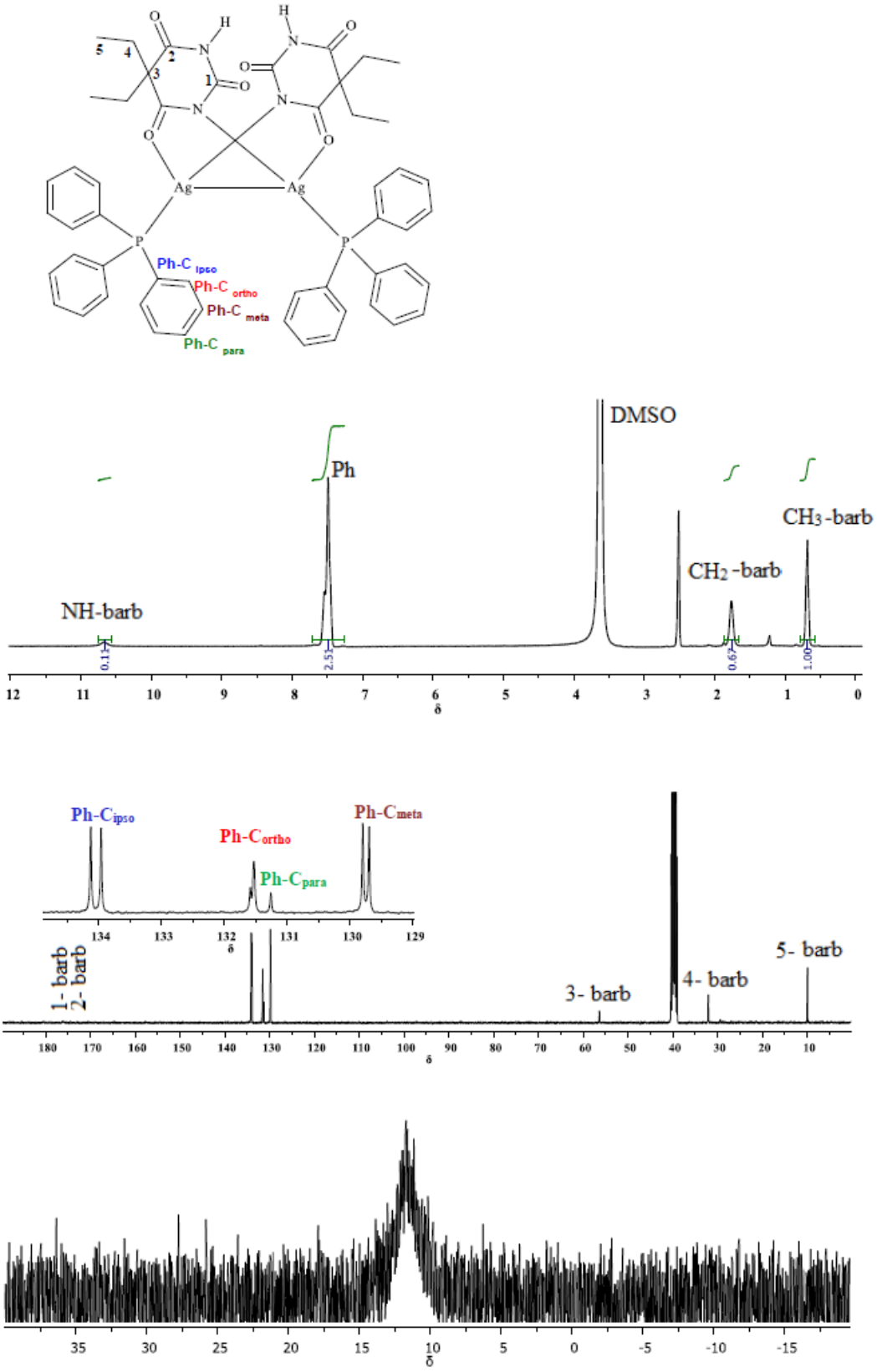


Fig. S2 continued

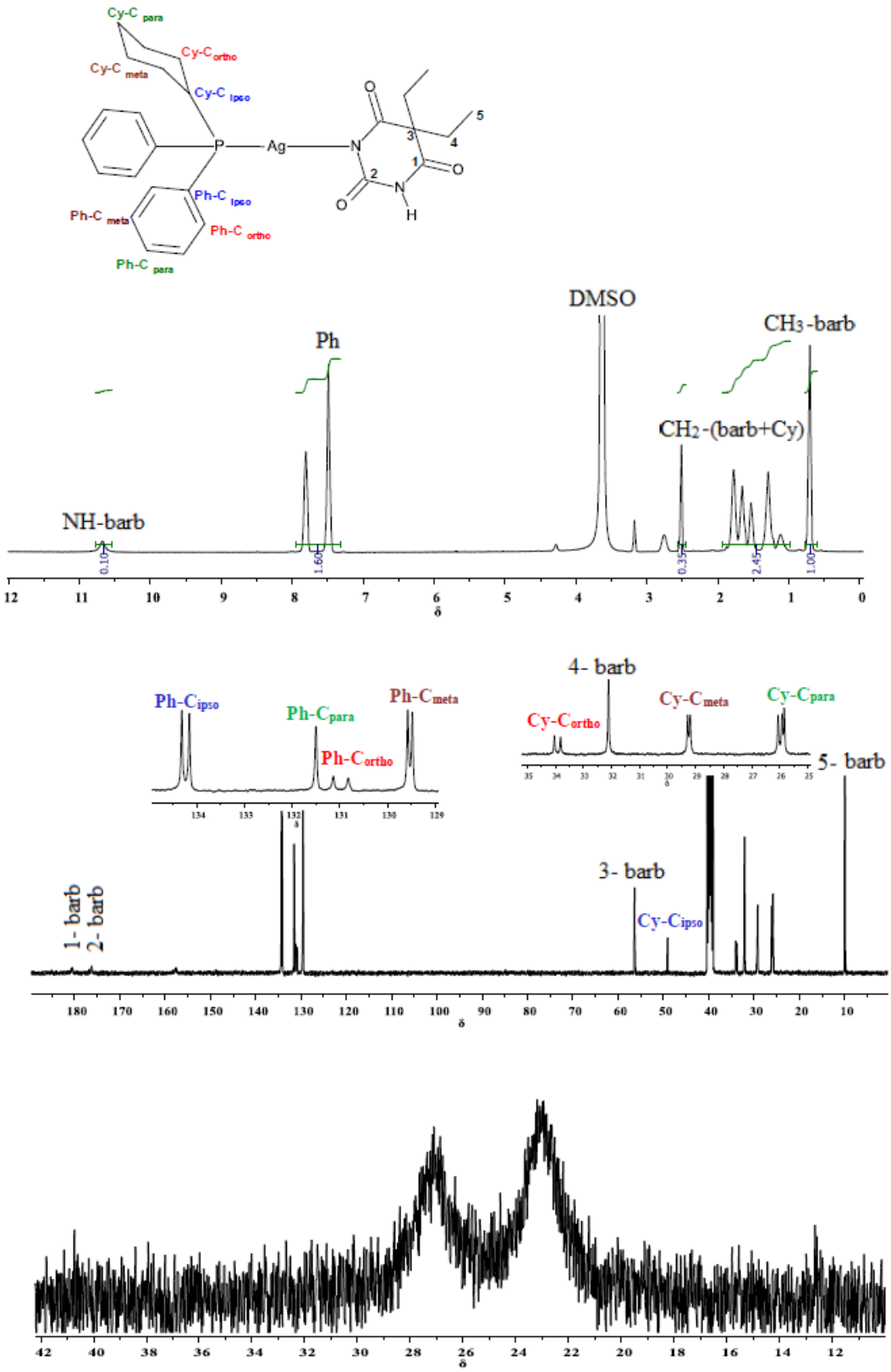


Fig. S2 continued

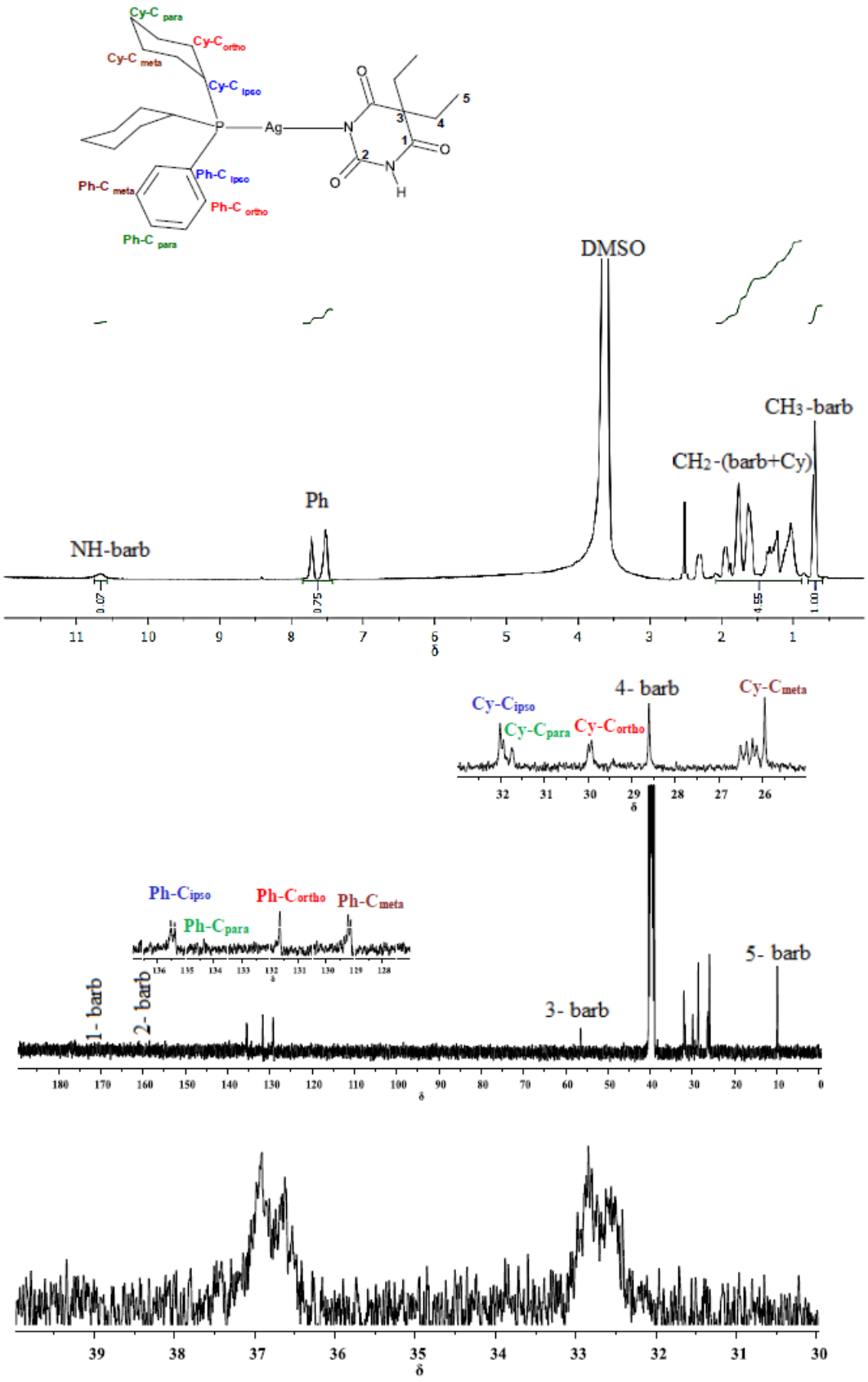


Fig. S2 continued

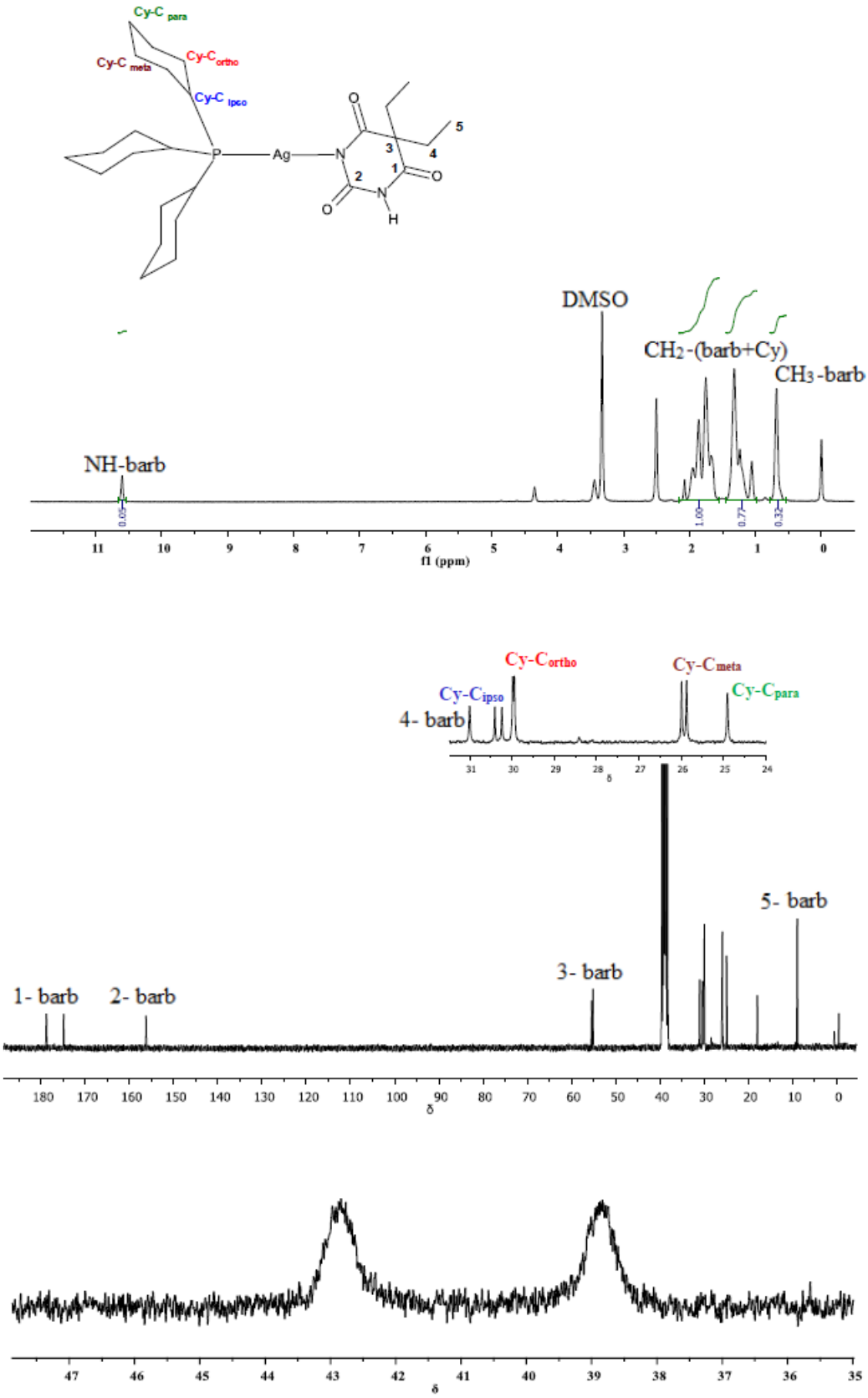


Fig. S2 ^{1}H-, ^{13}C- and ^{31}P-NMR spectra of **1**–**4**.

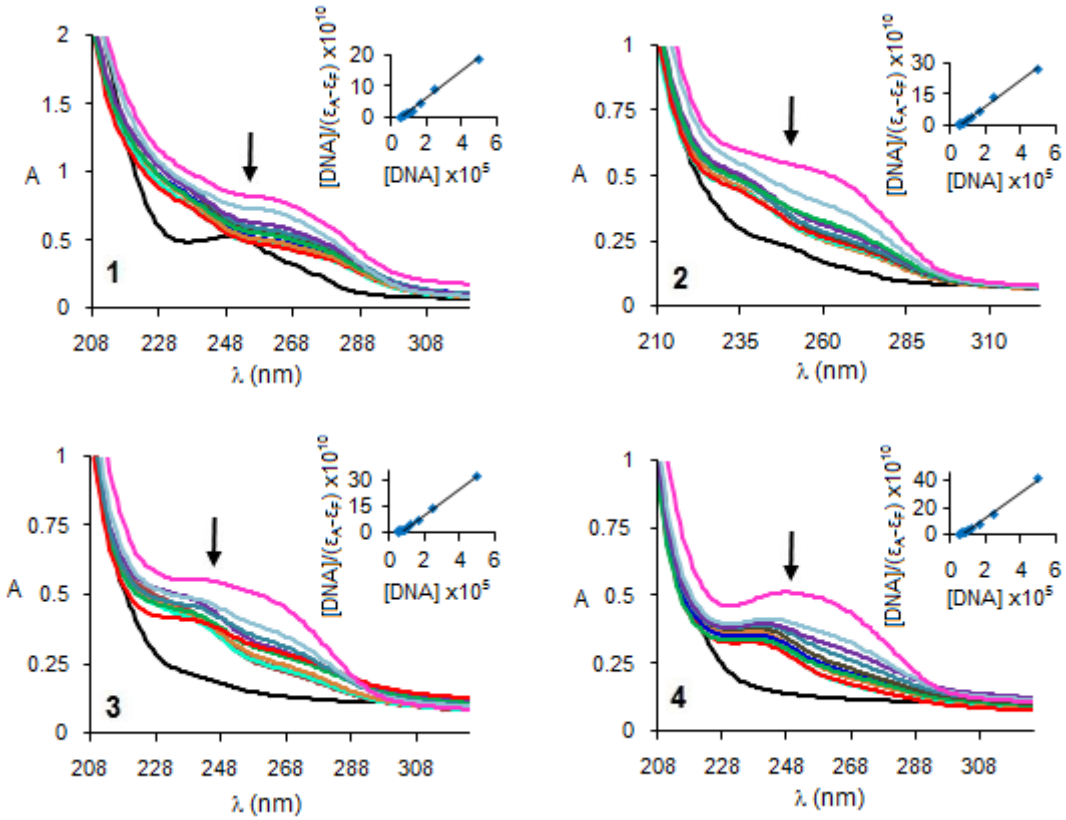


Fig. S3 UV spectra of **1**–**4** (10 µM) upon the titration of FS-DNA (0–50 µM) in Tris-HCl buffer. The arrow shows the decreases in absorbance with respect to an increase in the FS-DNA concentration. Inset: plot of [DNA]/($\varepsilon_a - \varepsilon_f$) vs. [DNA].

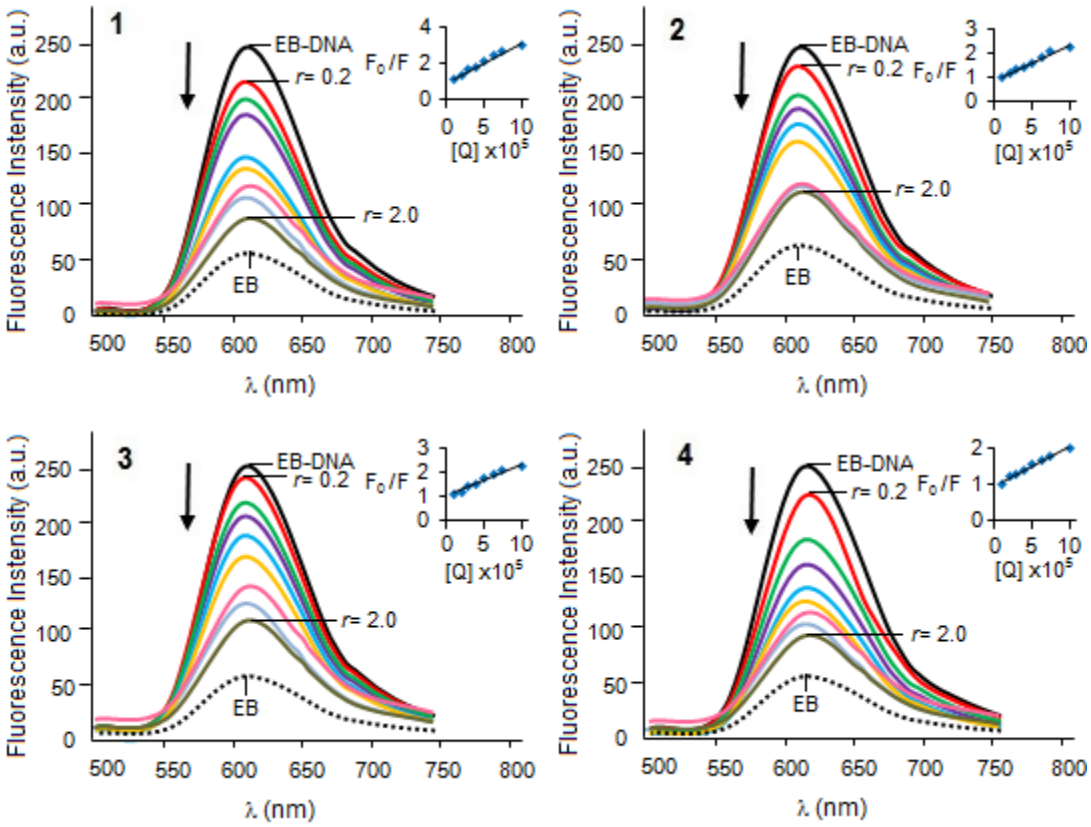


Fig. S4 Emission spectra of EB-bound FS-DNA solutions upon the titration of **1**–**4** (0–100 μM) in Tris-HCl buffer. [EB] = 5.0 μM, [DNA] = 50.0 μM, *r* = [complex]/[DNA]. The arrow shows the decreases in emission with increasing the concentration of **4**. Insets: Stern-Volmer plots of the fluorescence data.

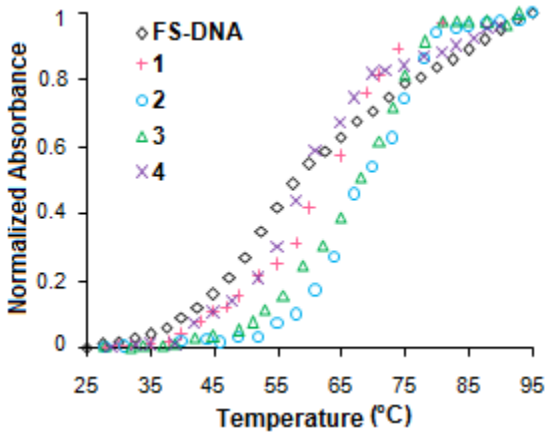


Fig. S5 Thermal denaturation profiles of FS-DNA (100 μM) in the absence and in the presence of **1**–**4** (50 μM) in Tris-HCl.

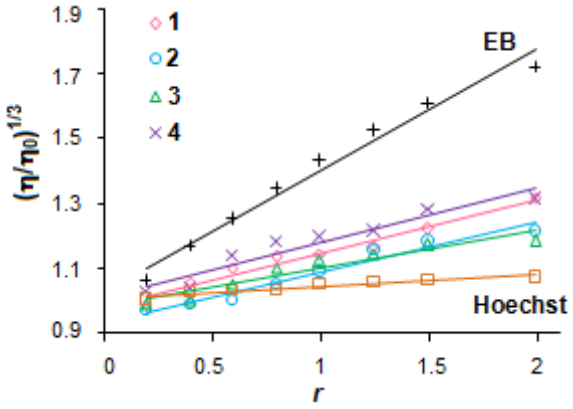


Fig. S6 The relative viscosity of FS-DNA upon addition of increasing amounts of complexes **1**–**4**, EB and Hoechst 33258 in Tris-HCl buffer. η is the viscosity of DNA in the presence of complex, and η_0 is the viscosity of DNA alone.

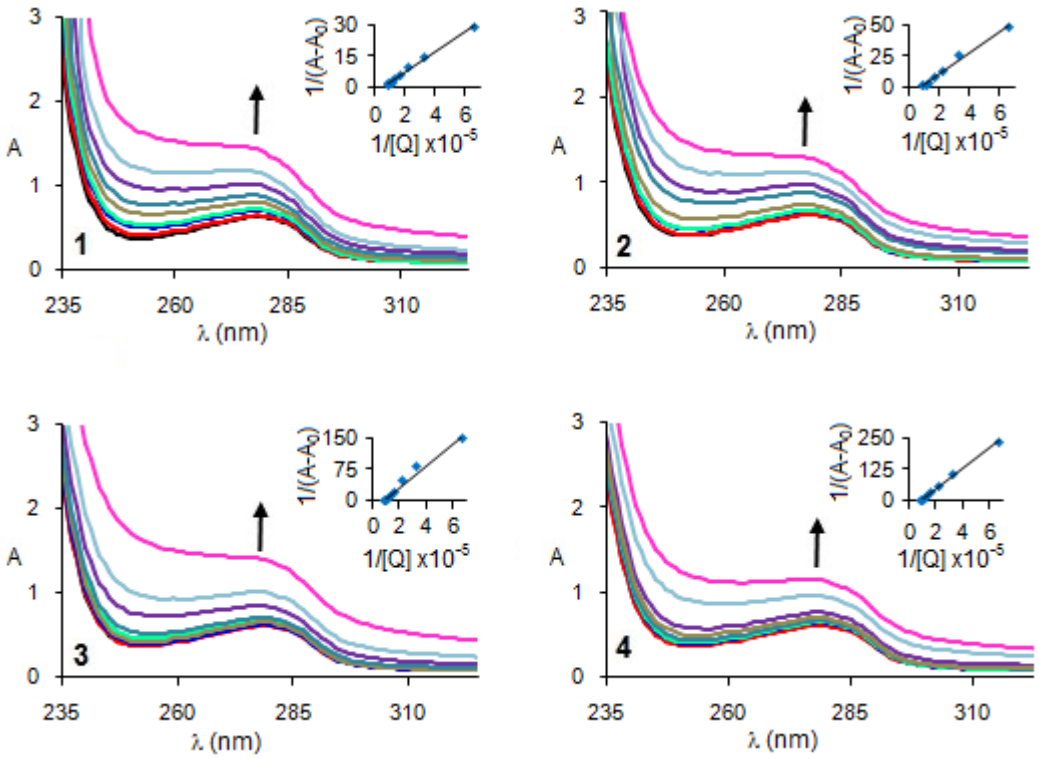


Fig. S7 UV absorption spectra of BSA (15 μM) upon addition of increasing amounts of complexes **1**–**4** (0–12 μM) in Tris-HCl buffer. The arrow shows the increases in absorbance. Inset: plot of 1/[complex] vs. 1/(A–A_0).

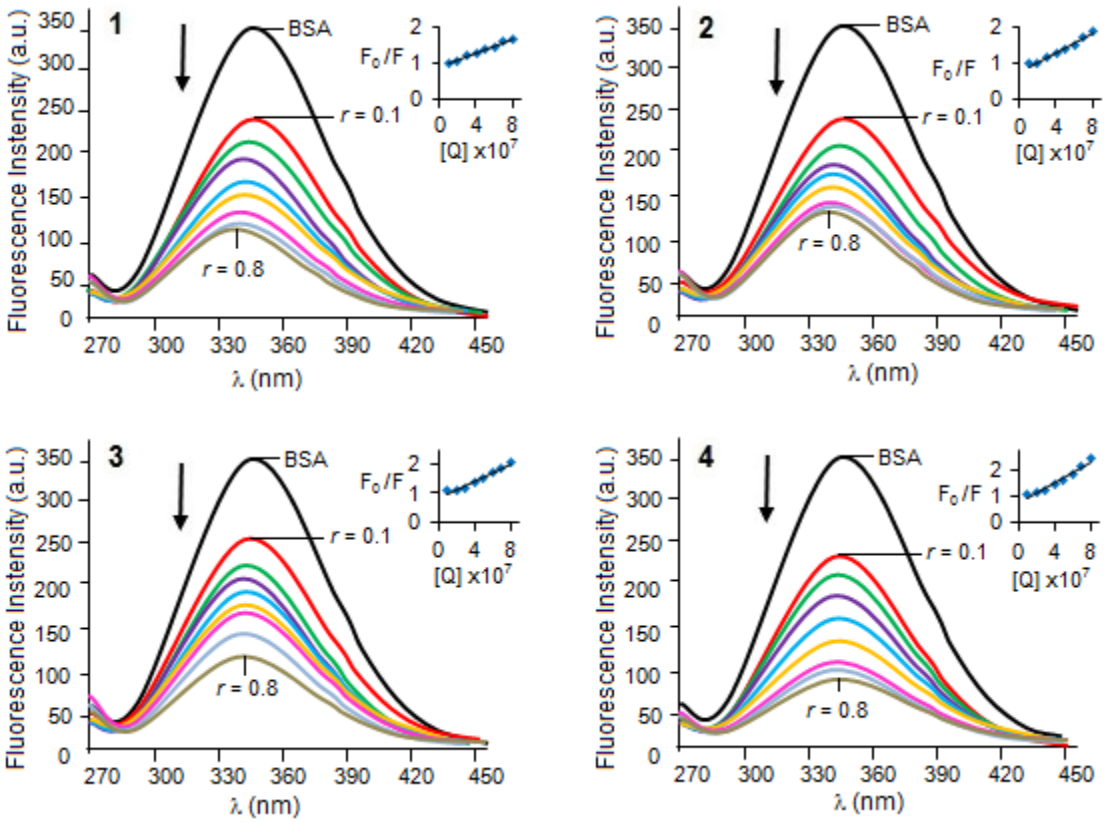
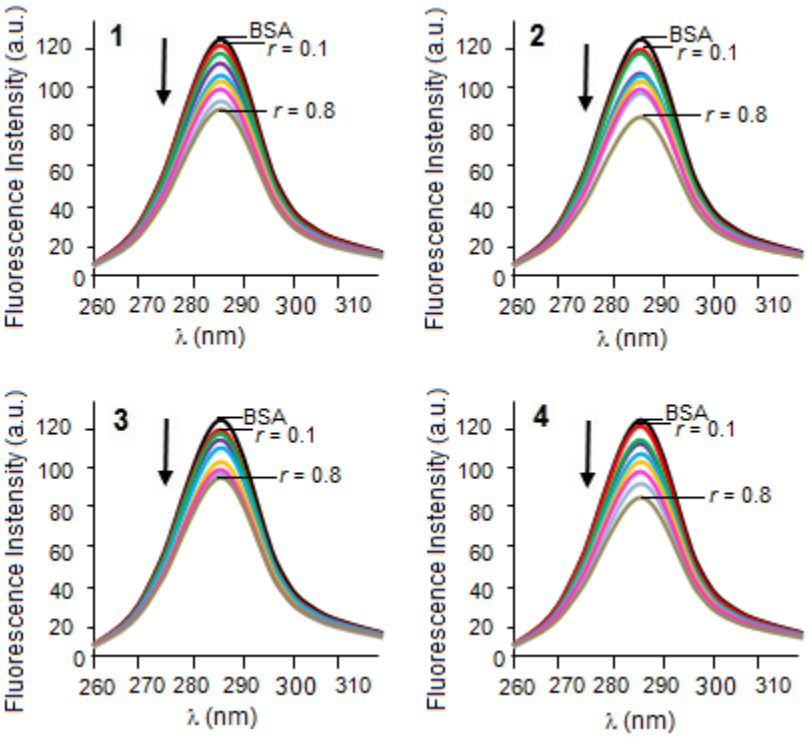
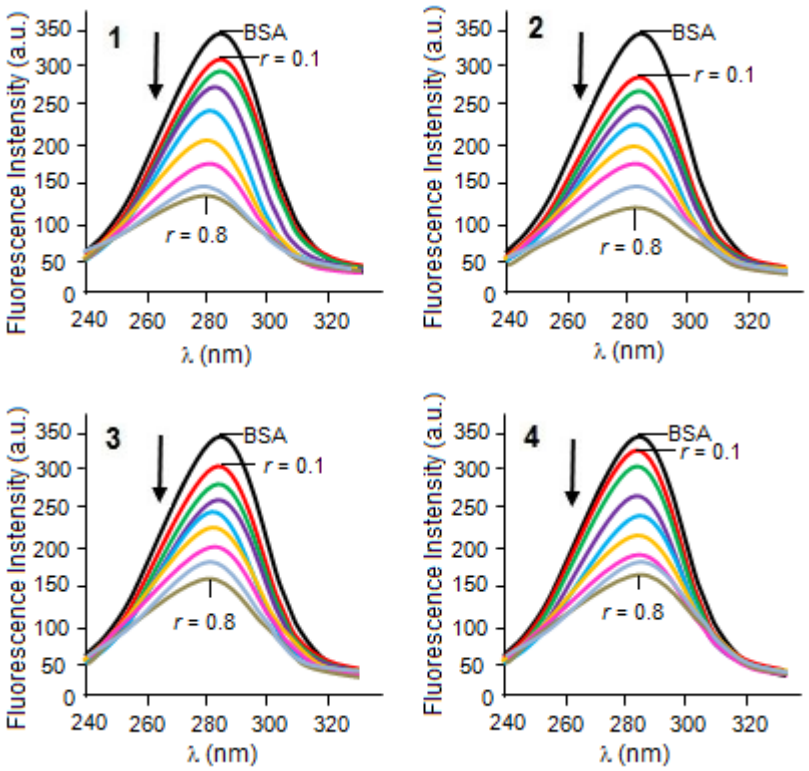


Fig. S8 Emission spectra of BSA (1.0 μM; λex = 280 nm) in presence of **1–4** (0-8.0 μM). The arrow shows the emission intensity changes upon increasing complex concentration. Insets: Stern-Volmer plot of the fluorescence data.



(**a**)



(**b**)

Fig. S9 Synchronous spectra of BSA (1.0 μM) in presence of **1**–**4** (0-8.0 μM) at Δλ = 15 nm (**a**) and Δλ = 60 nm (**b**). Arrows show the emission intensity changes upon increasing concentration of **1**–**4**.

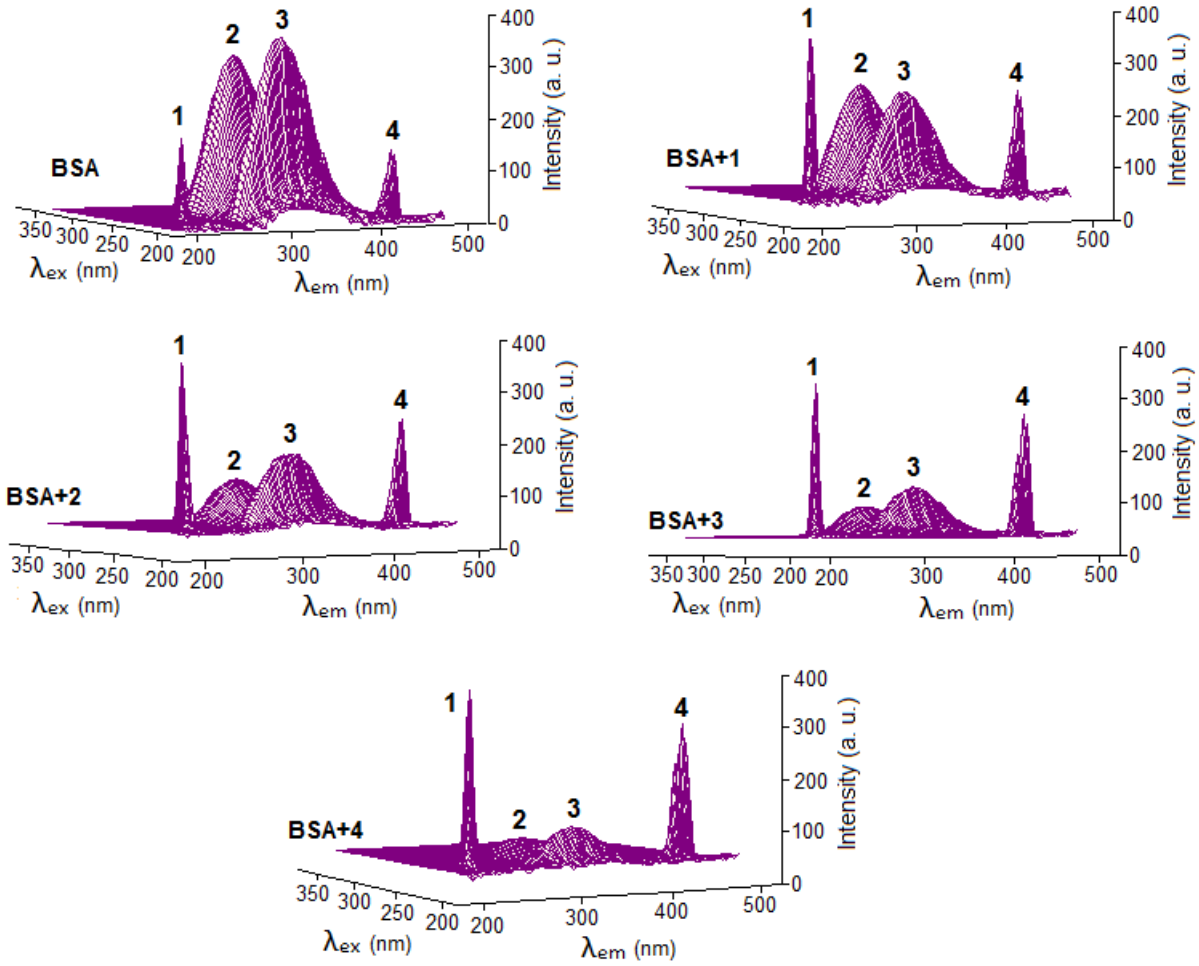


Fig. S10 3D fluorescence spectra of BSA (2 μM) and BSA (2 μM) + **1**–**4** (2 μM) in Tris-HCl buffer.

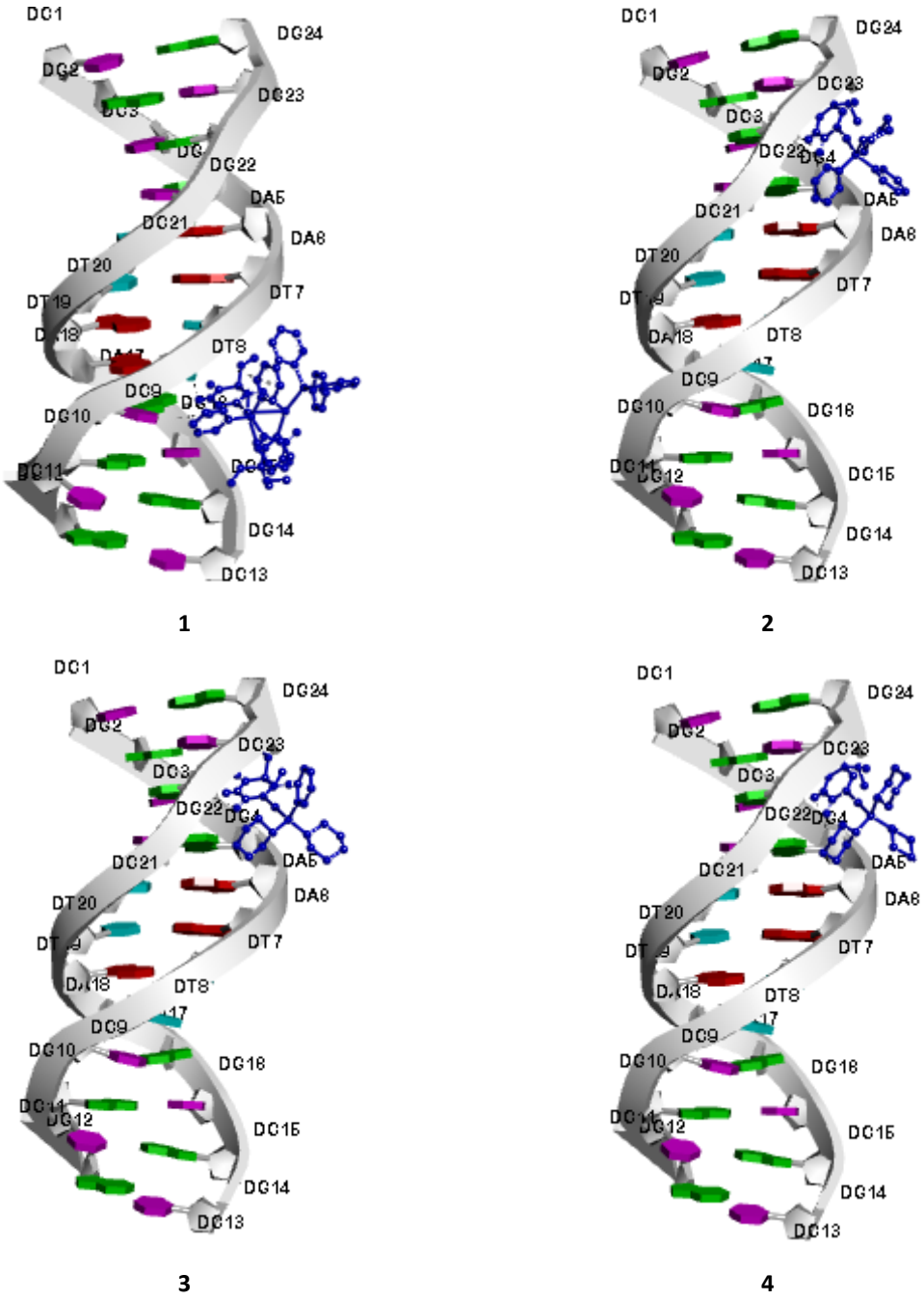


Fig. S11 Molecular docked model of **1**–**4** located within the grooves of DNA (1BNA).

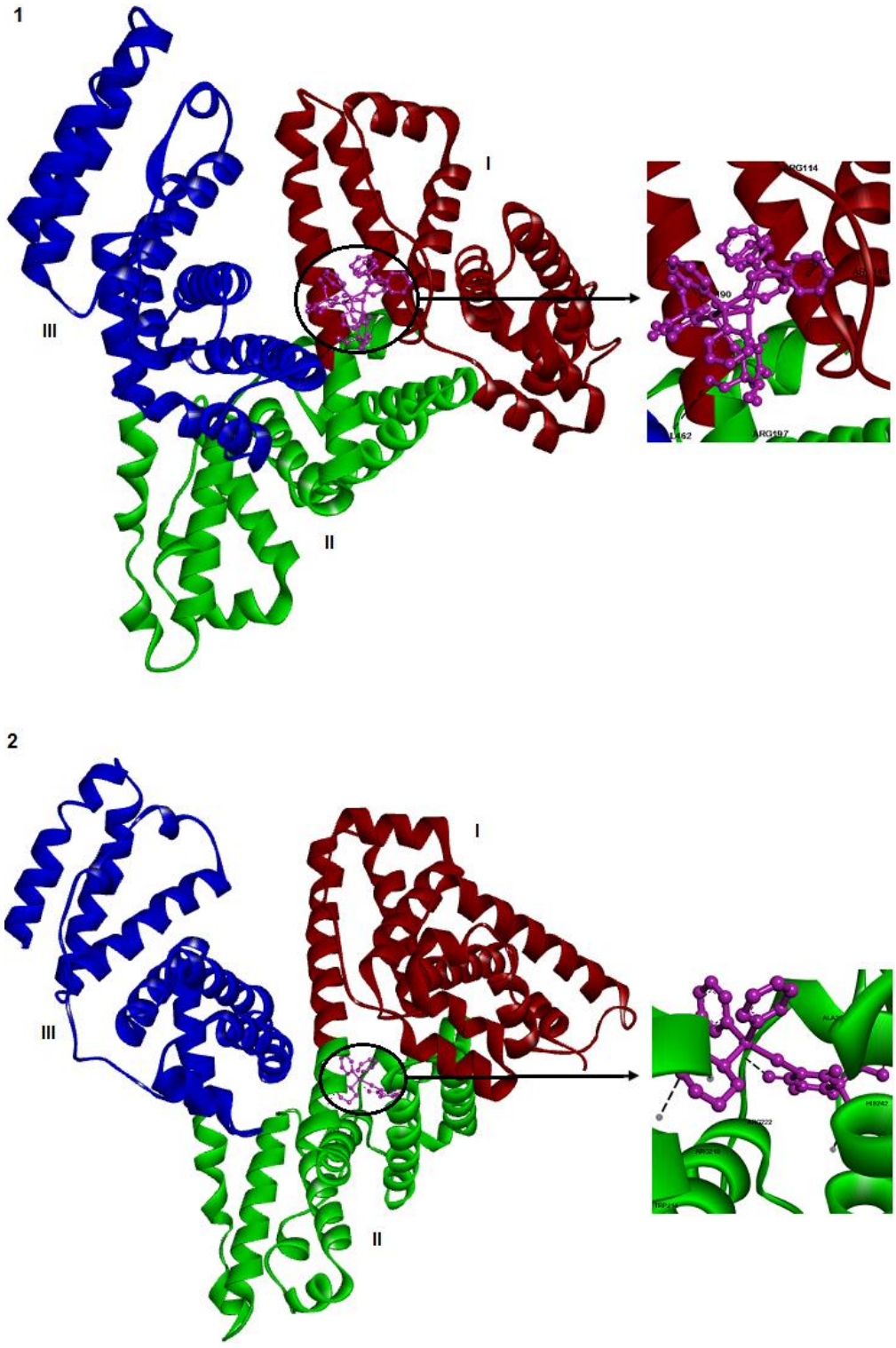


Fig. S12 Continued

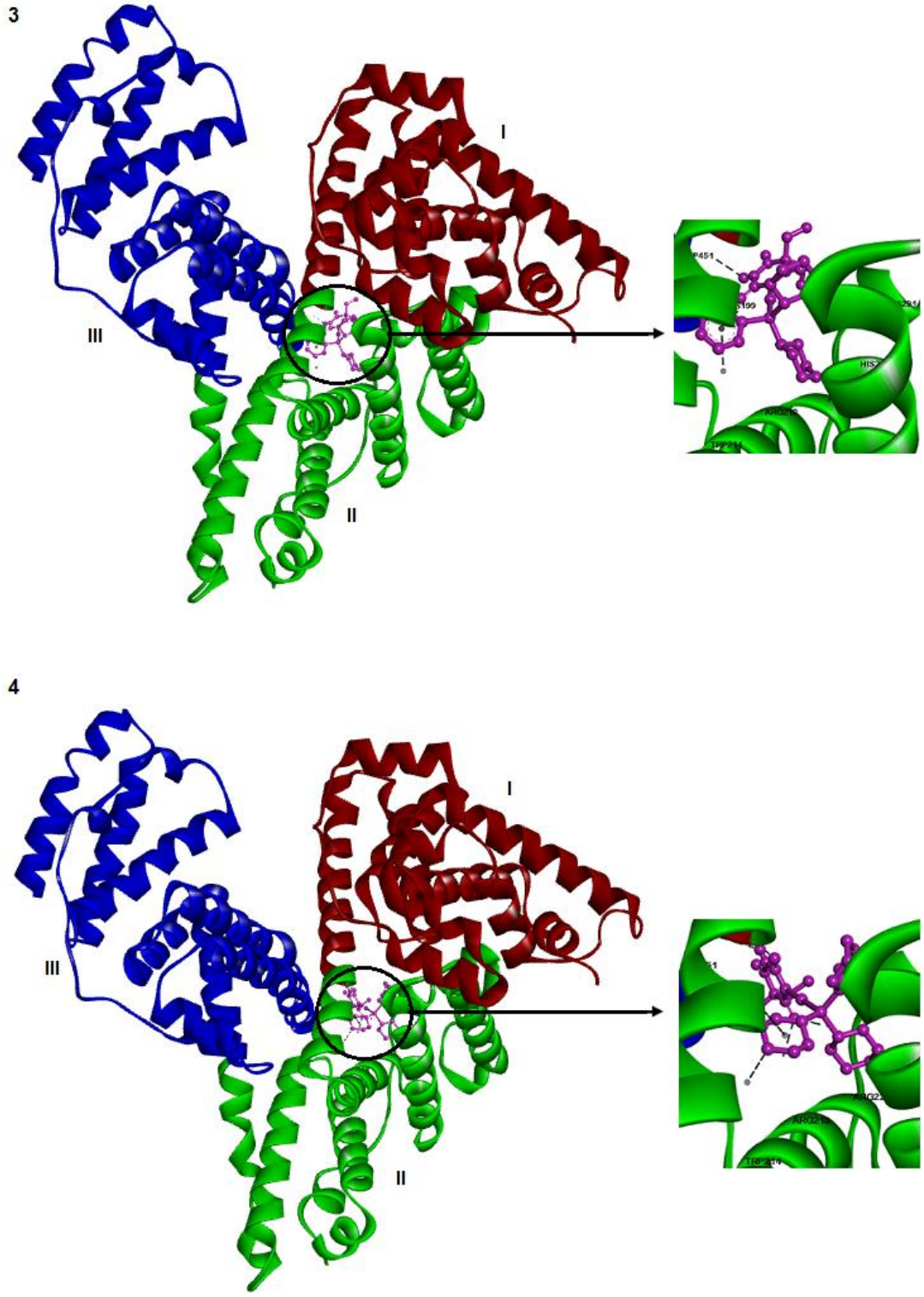


Fig. S12 Molecular docked model of **1**–**4** located within the hydrophobic cavity of HSA (1H9Z).

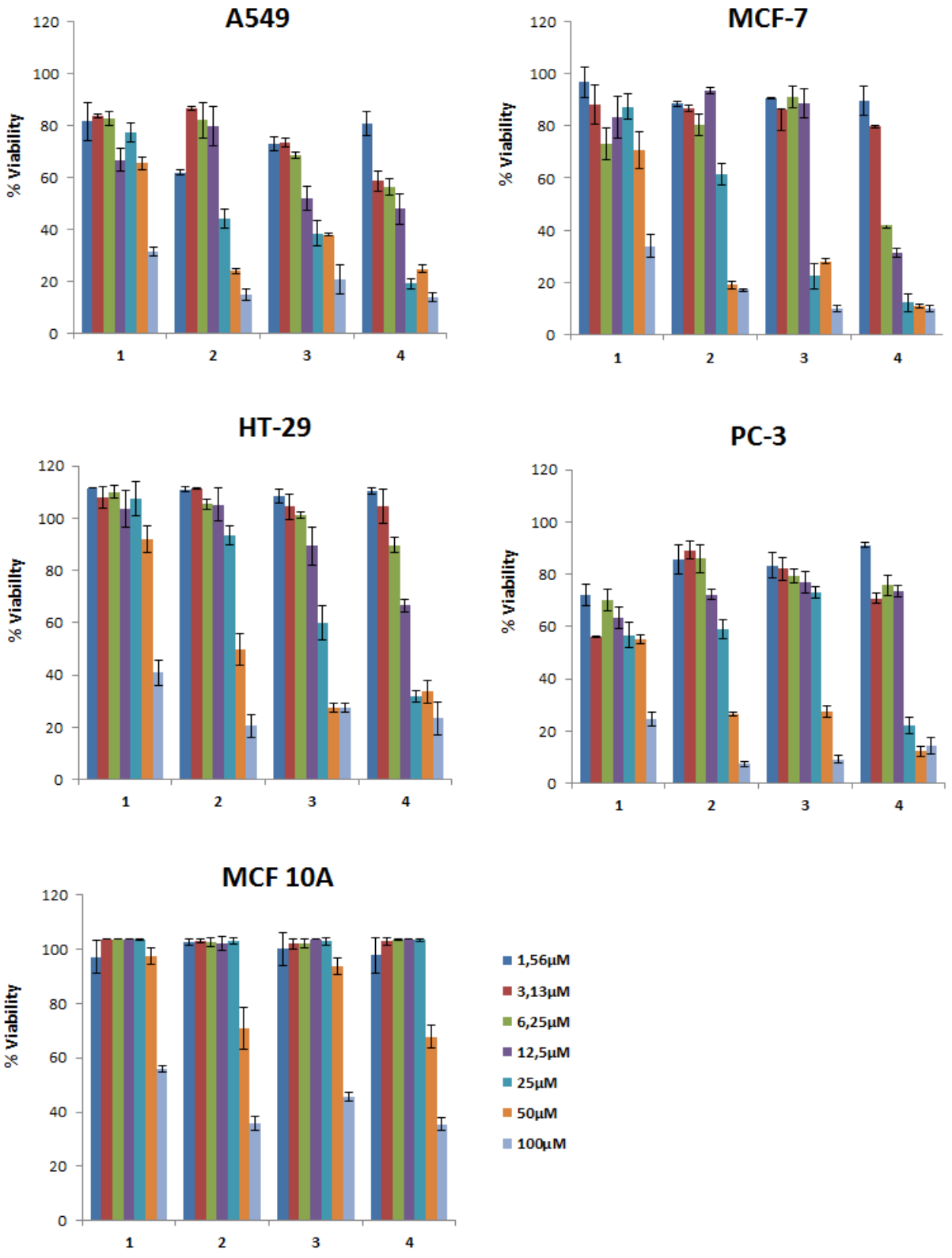


Fig. S13 The dose-response graphics for **1**–**4** obtained from SRB assay, showing the effect of the complexes on the growth of the cell lines after 48 h of treatment.