Supplementary Information

Water soluble ionic Co(II), Cu(II) & Zn(II) diimine-glycinate complexes targeted to tRNA: Structural description, *in vitro* comparative binding, cleavage and cytotoxic studies towards chemoresistant prostate cancer cells

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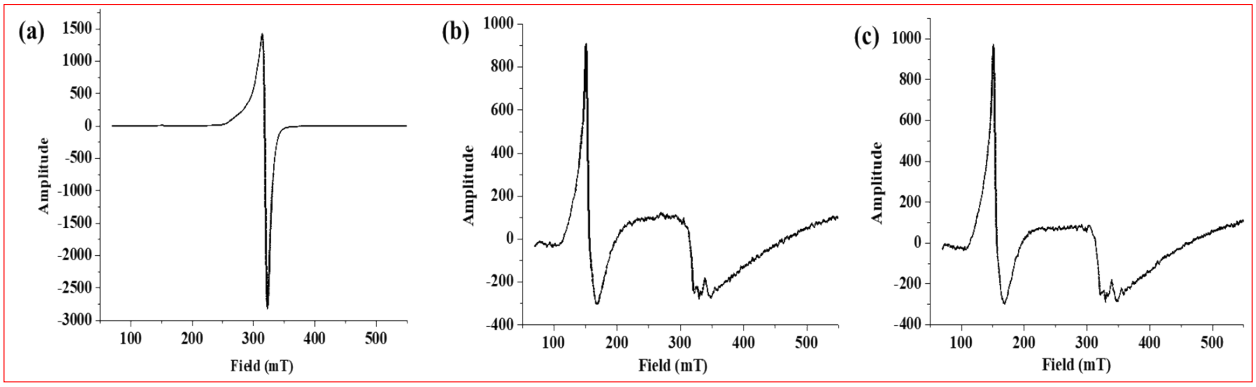
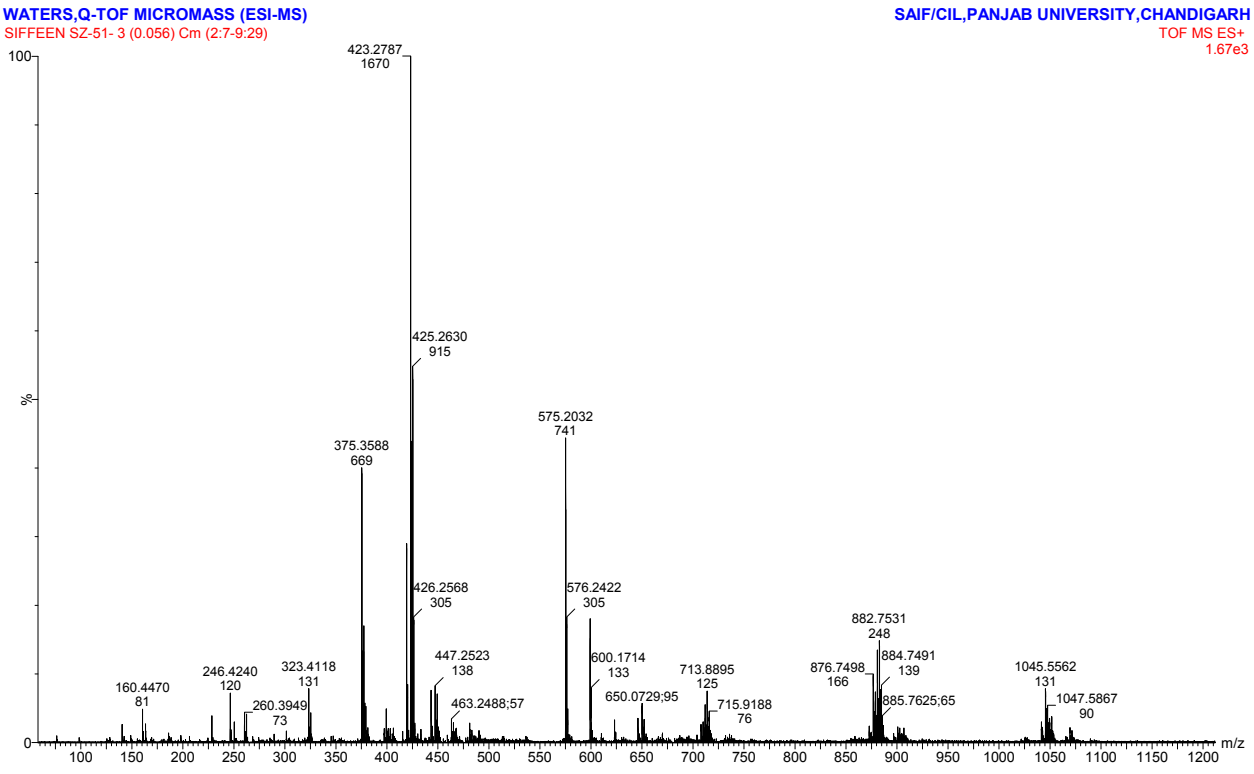


Fig. S1. EPR spectra of complexes **1**, **2** and **4** at Liquid Nitrogen Temperature.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SAIF/CIL,PANJAB UNIVERSITY,CHANDIGARH
TOF MS ES+
1.67e3
423.2787 1670
425.2630 915
575.2032 741
375.3588 669
426.2568 305
576.2422 305
882.7531 248
447.2523 138
600.1714 133
884.7491 139
876.7498 166
713.8895 125
1045.5562 131
323.4118 131
246.4240 120
160.4470 81
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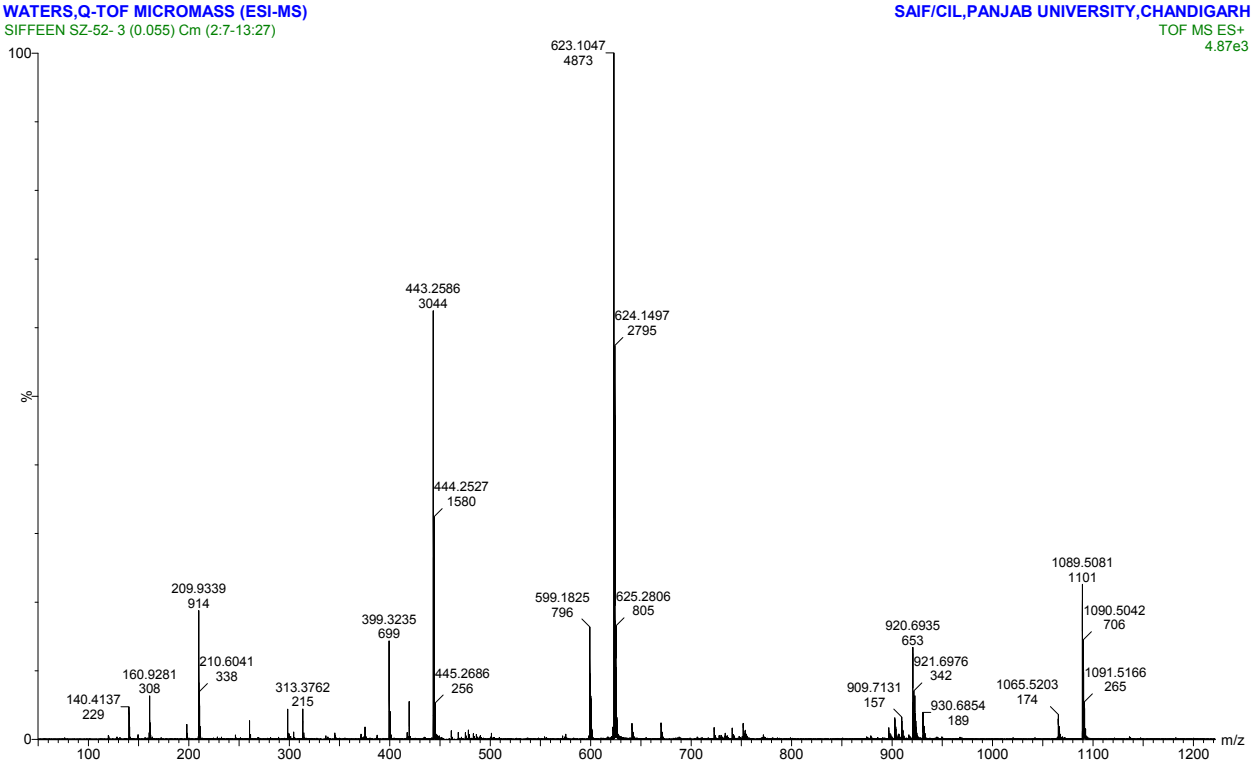
650.0729;95
715.9188 76
885.7625;65
1047.5867 90
%
m/z

(1)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443.2586 3044
624.1497 2795
444.2527 1580
1089.5081 1101
209.9339 914
599.1825 796
625.2806 805
1090.5042 706
399.3235 699
920.6935 653
921.6976 342
210.6041 338
160.9281 308
445.2686 256
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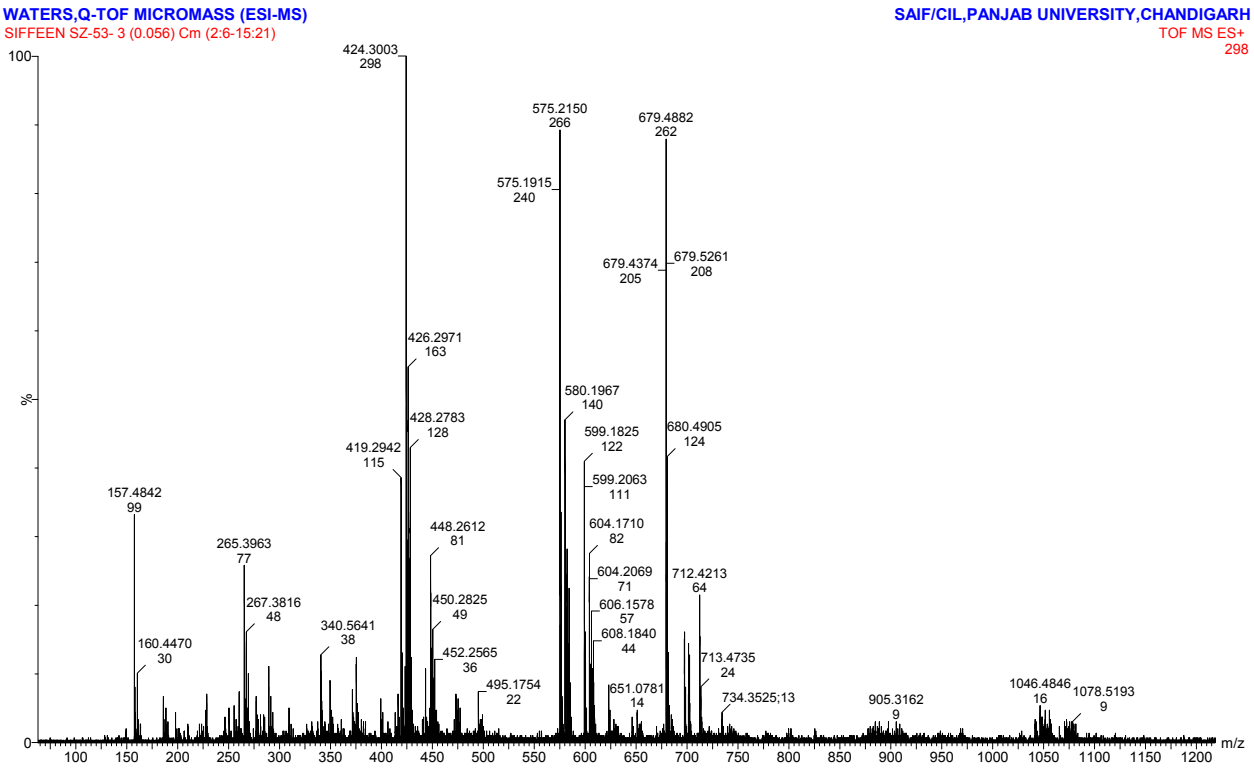
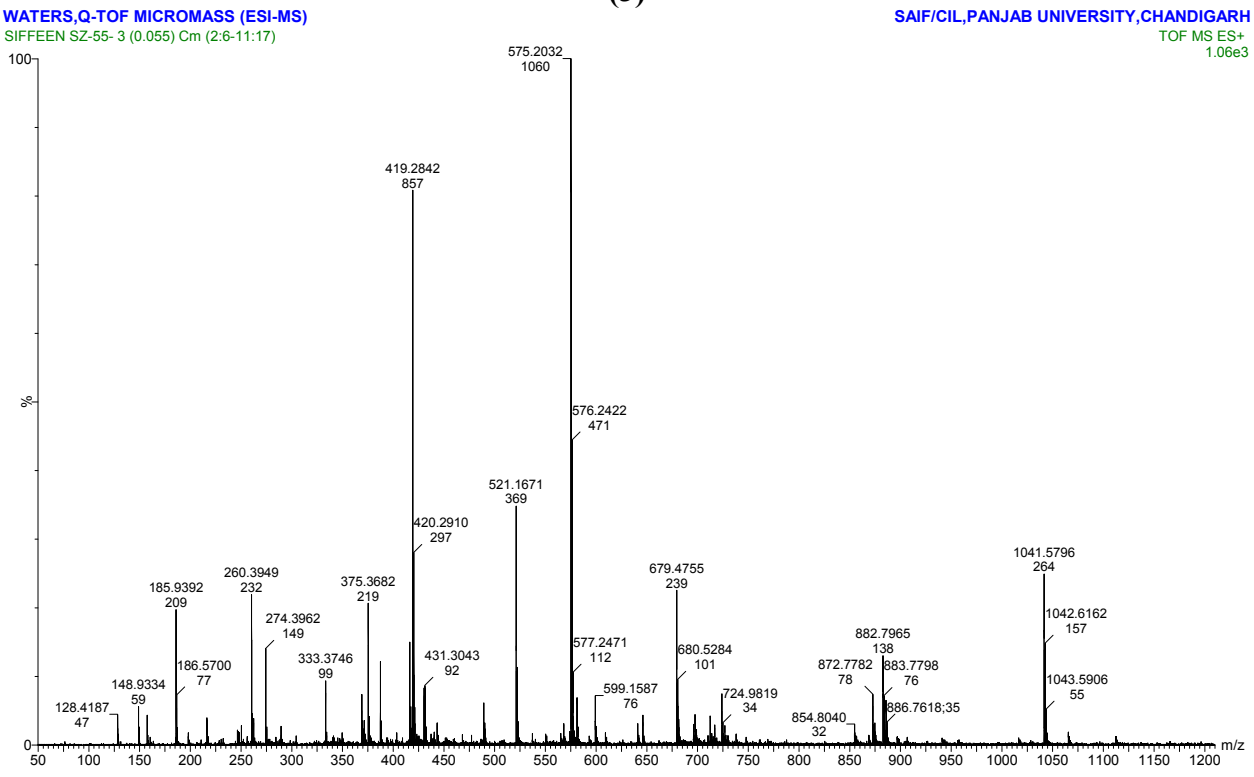
%
m/z

(2)

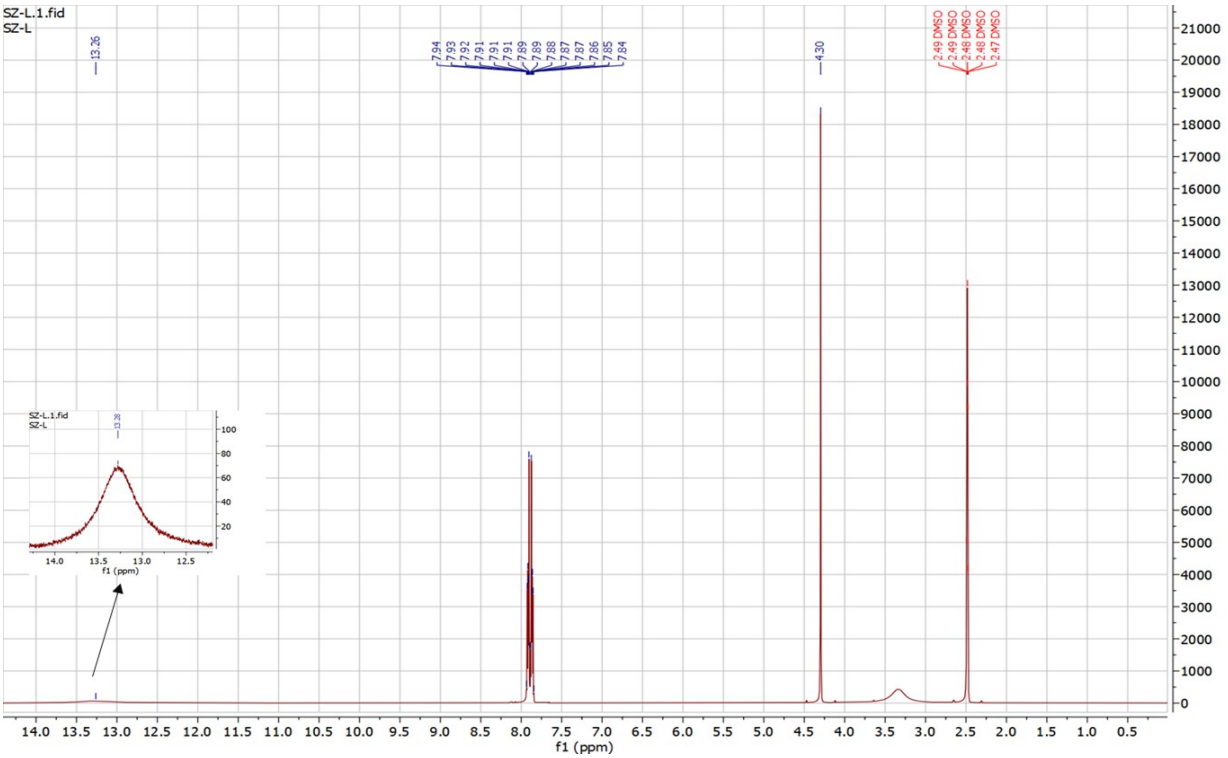


(3)

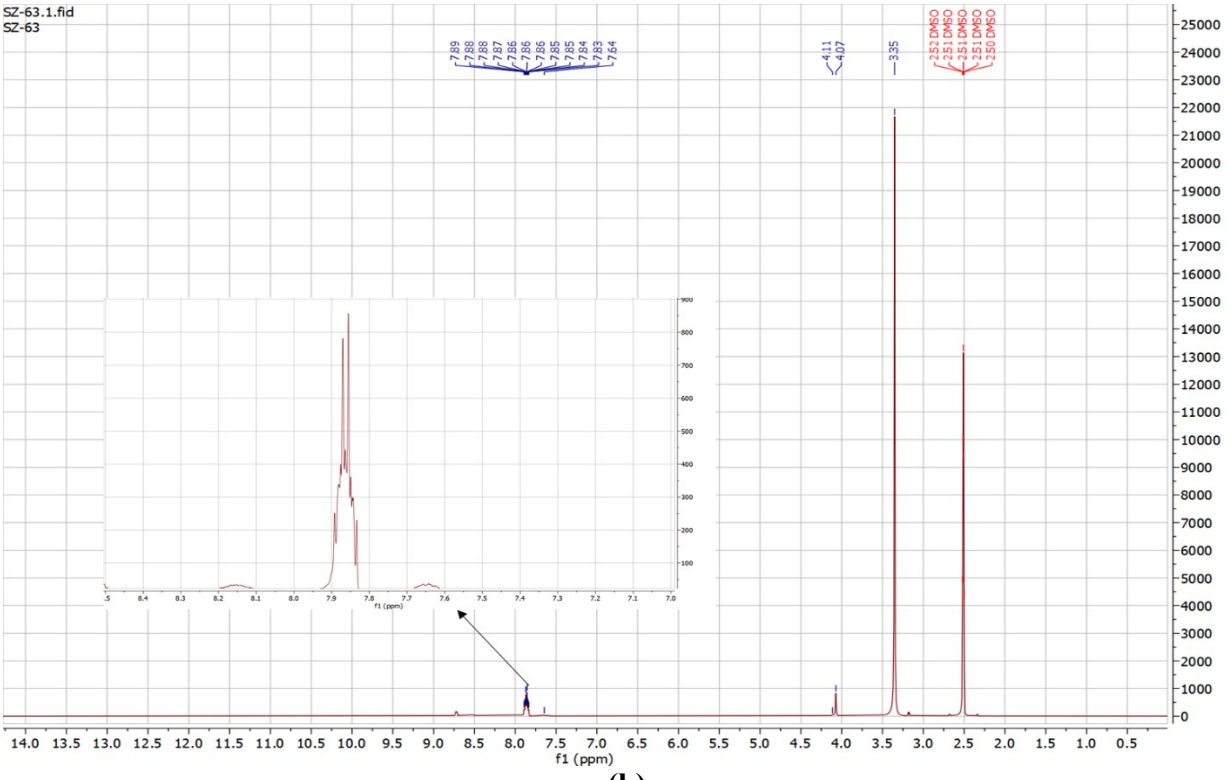


(4)

Fig. S2. Mass spectra of complexes **1**–**4**.

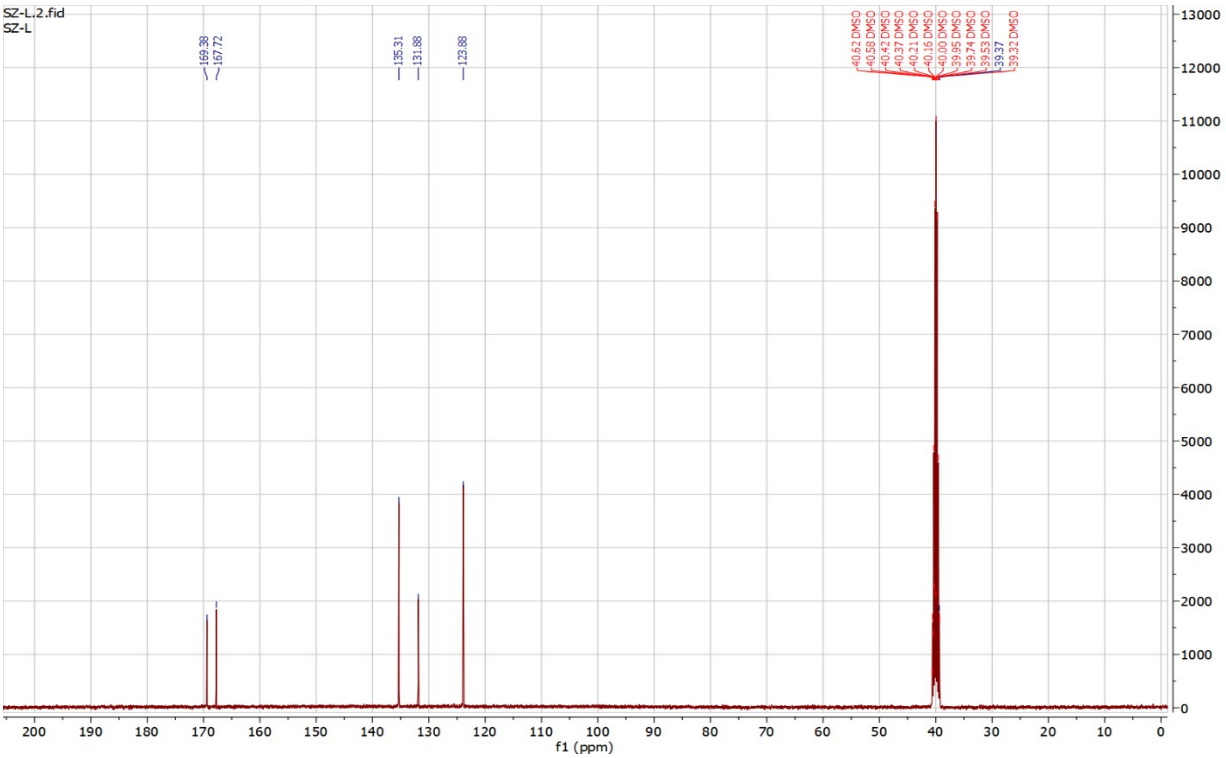


(a)

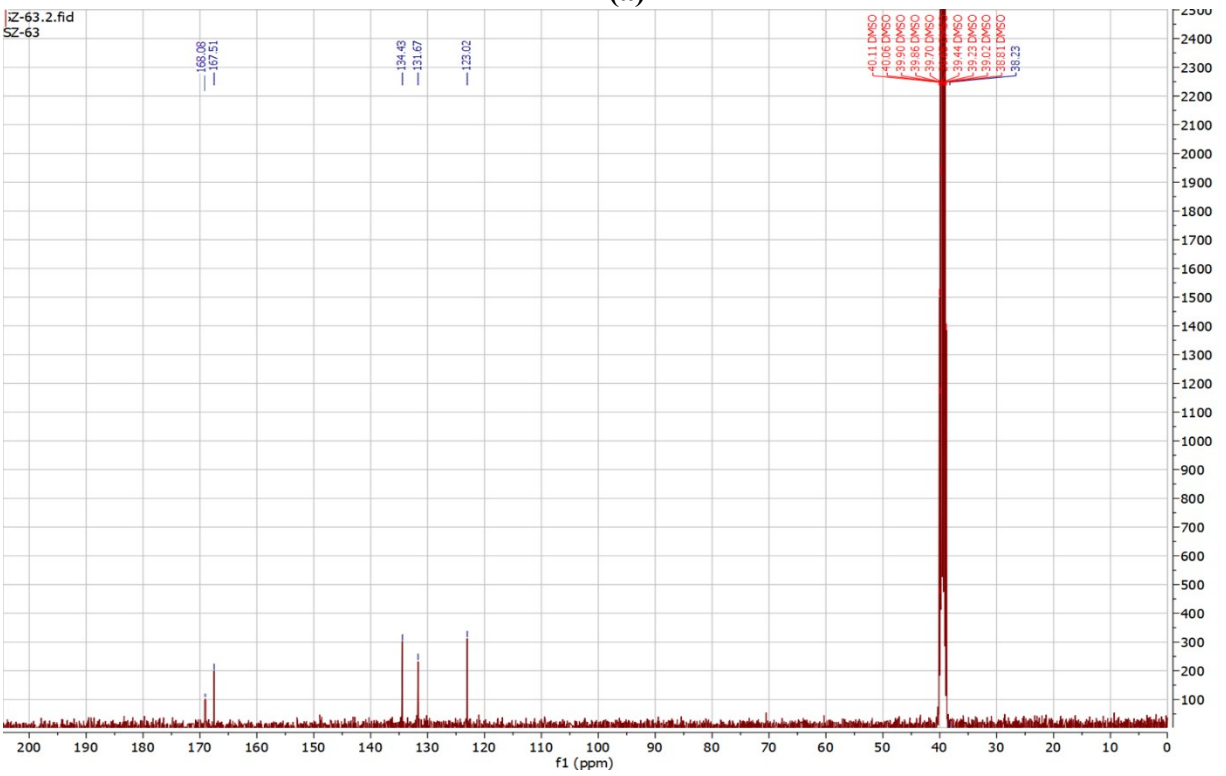


(b)

Fig. S3. ^{1}H spectra of the (a) ligand Phthaloylglycine and (b) complex **3**.



(a)



(b)

Fig.**S4.** ^{13}C NMR spectra of the (a) ligand Phthaloylglycine and (b) complex **3**.

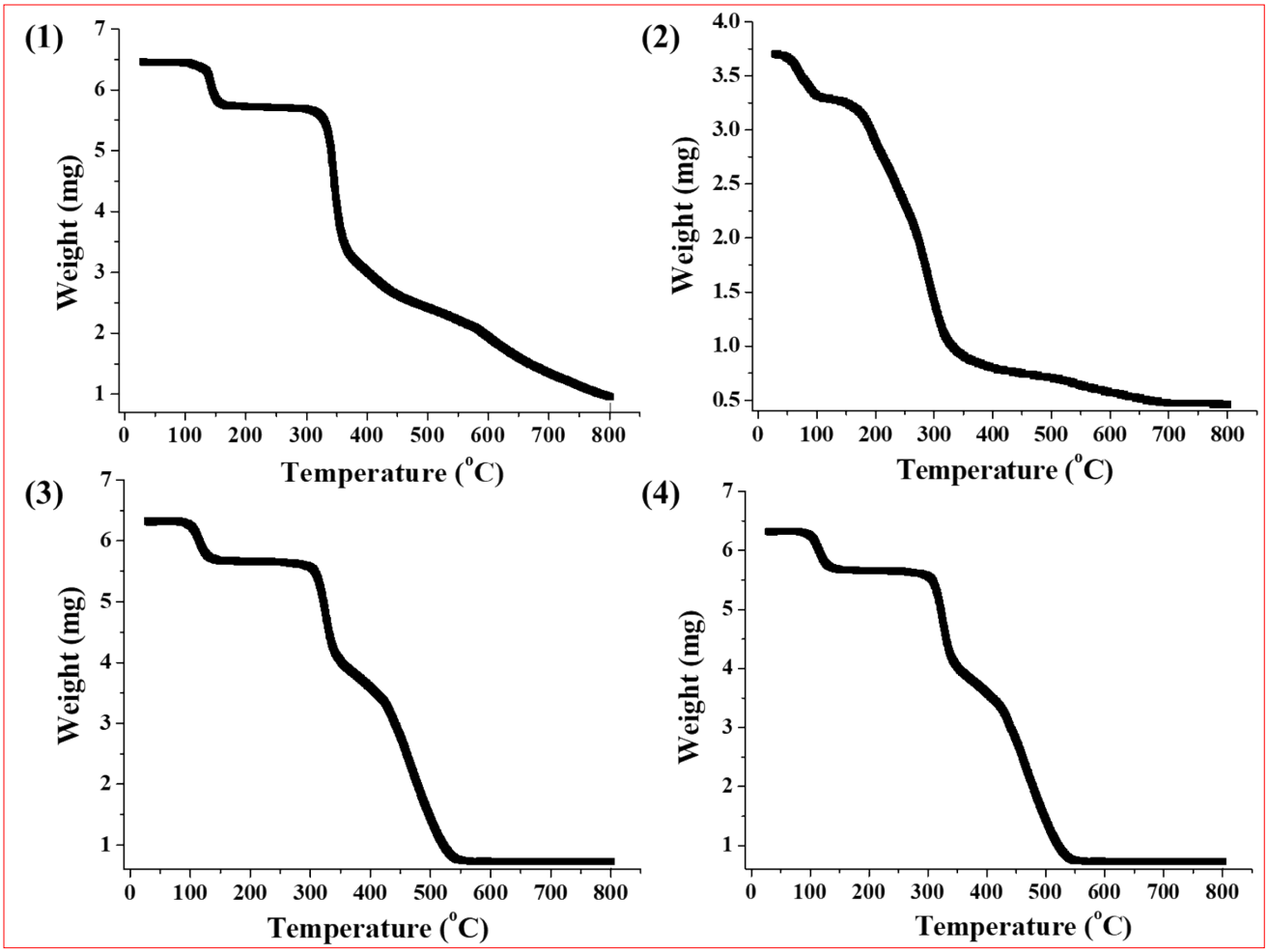


Fig.**S5.** Themogravimetric analysis (TGA) curves for complexes **1**–**4**.

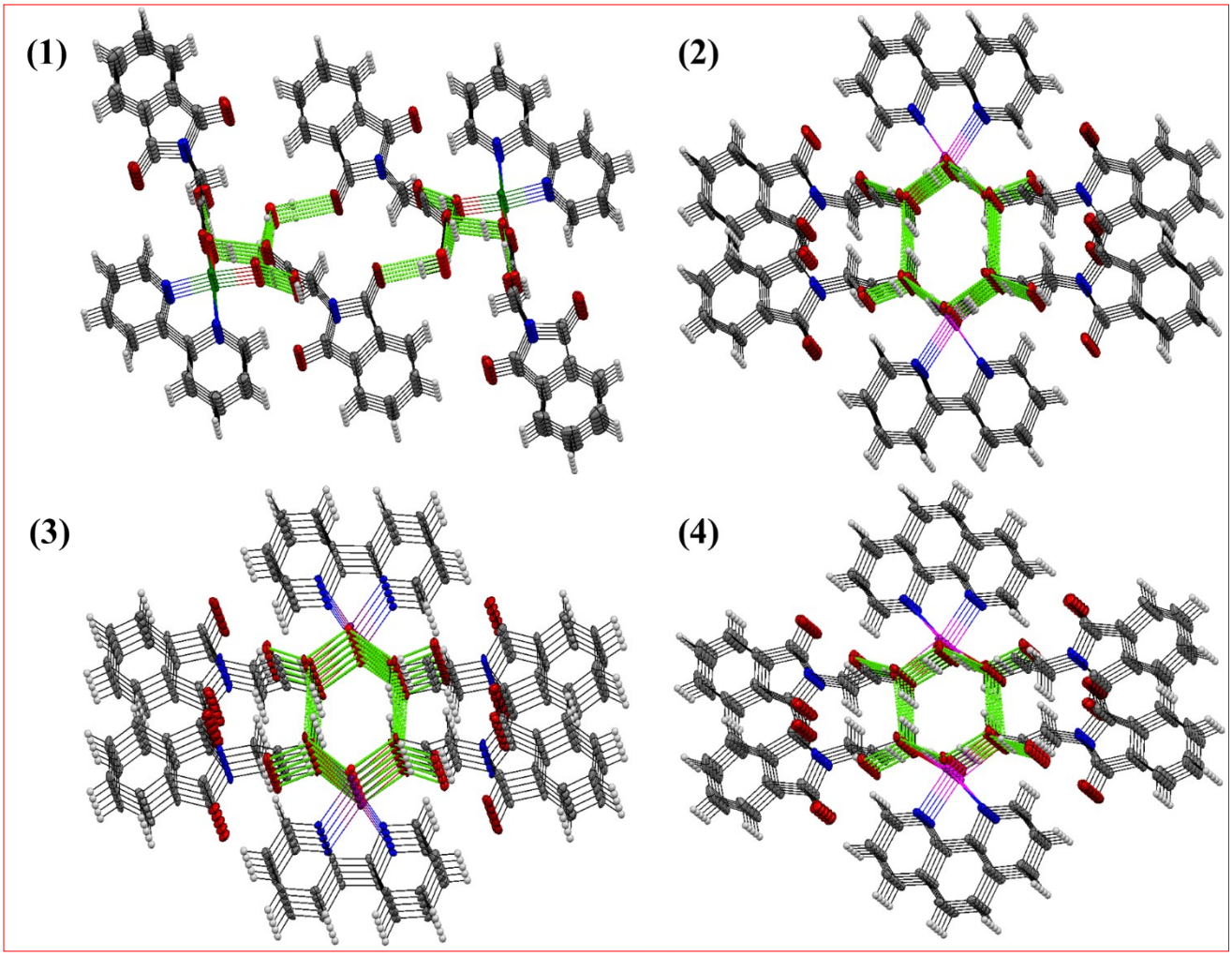


Fig. S6. Intermolecular C–H----O hydrogen bonding (shown by green color) resulting in 2–dimensional architectures in complexes **1**–**4**.

Table S1. Crystallographic data of complexes **1–4.**

Complex	**1**	**2**	**3**	**4**
CCDC	1965359	1965362	1965360	1965363
Empirical formula	C_{30} $H_{26}CuN_4O_{13}$	$C_{30}H_{28}CoN_4O_{12}$	$C_{30}H_{24}N_4O_{12}Zn$	$C_{32}H_{28}CoN_4O_{12}$
F_w (gmol^{-1})	714.10	695.49	697.92	719.51
Temperature (K)	150	150	150	150
Crystal system	Triclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*P -1*	*C2/c*	*C2/c*	*C 2/c*
a (Å)	7.1549(6)	32.8560(15)	32.858(3)	32.6329(15)
b (Å)	13.9178(9)	12.1150(6)	12.1027(10)	12.9695(4)
c (Å)	16.9211(12)	7.2898(3)	7.3119(9)	7.2447(3)
α (°)	110.138(2)	90	90	90
β (°)	100.826(3)	94.678(2)	94.642(4)	94.143(2)
γ (°)	91.382(2)	90	90	90
Volume (Å^3)	1546.6(2)	2892.0(2)	2898.2(5)	3058.2(2)
Z	2	4	4	4
ρ_{calc} (g cm^{-3})	1.533	1.597	1.599	1.563
μ (mm^{-1})	0.781	0.670	0.923	0.636
F(000)	734	1436	1432	1484
Crystal size (mm)	0.21x0.15x0.15	0.16 x 0.12x 0.12	0.19x 0.18 x 0.15	0.18x 0.18 x 0.17
θ Range (°)	2.373−26.441	2.488−28.818	2.488−26.431	2.488–25.242
Completeness (%)	0.998	0.987	0.998	0.998
Measured reflections	26494	23999	21318	41234
Independent reflections/ R_{int}	6347/0.1127	3722/ 0.0419	2985/0.1268	3955/0.0395
Observed reflectios [I>2σ(I)]	4668	3303	2370	3623
Data / restraints / parameters	/9/442	3722 / 6 / 229	2985 /3/216	3955/6/238
Goodness-of-fit on F^2	1.019	1.061	1.185	1.065
Final indices [I>2sigma(I)]	R1 = 0.0587 wR2 = 0.1351	R1 = 0.0279 wR2 = 0.0662	R1 = 0.0743 wR2 = 0.1750	R1 = 0.0269 wR2 = 0.0724
R indices (all data)	R1 = 0.0901 wR2 = 0.1522	R1 = 0.0343 wR2 = 0.0689	R1 = 0.0975 wR2 = 0.1850	R1 = 0.0300 wR2 = 0.0740
Largest diff. peak/hole (eÅ^{-3})	1.438/–1.024	0.366/–0.376	2.456/–0.893	0.265/–0.541

Table S2. Selected bond length of complexes **1–4** in Angstrom (Å).

Complex 1			
Atoms	**Bond length (Å)**	**Atoms**	**Bond length (Å)**
Cu1–N1	2.016(3)	O7–C21	1.254(5)

Cu1–N2	1.990(3)	O8–C21	1.246(5)
Cu1–O1	1.954(3)	O5–H5O(A)	0.944(19)
Cu1–O5	1.950(3)	O6–H6O(B)	0.929(19)
Cu1–O6	2.261(3)	O6–H6O(A)	0.931(19)
O1–C11	1.281(5)	O5–H5O(B)	0.930(19)
O2–C11	1.225(5)		
Complex 2			
Atoms	**Bond length (Å)**	**Atoms**	**Bond length (Å)**
Co1–N1	2.1380(11)	O1–C6	1.2362(16)
Co1–O5	2.0606(9)	O2–C6	1.2807(16)
Co1–O6	2.1227(10)		
Complex 3			
Atoms	**Bond length (Å)**	**Atoms**	**Bond length (Å)**
Zn1–O6	2.117(4)	O1–C6	1.290(7)
Zn1–O5	2.125(4)	O2–C6	1.227(7)
Zn1–N1	2.157(4)		
Complex 4			
Atoms	**Bond length (Å)**	**Atoms**	**Bond length (Å)**
Co1–O5	2.0228(9)	O1–C7	1.2342(15)
Co1–N1	2.1632(10)	O2–C7	1.2809(13)
Co1–O6	2.1634(8)		

Table S3. Selected bond angles of complexes **1**–**4** in degree (°).

Complex 1			
Atoms	**Bond angle (°)**	**Atoms**	**Bond angle (°)**
O5–Cu1–O1	89.65(11)	Cu1–O5–H5OA	119(3)
O5–Cu1–N2	173.65(12)	Cu1–O5–H5OB	109(3)
O1–Cu1–N2	94.18(12)	Cu1–O6–H6OA	90(3)
O5–Cu1–N1	93.28(12)	Cu1–O6–H6OB	113(4)
O1–Cu1–N1	154.55(12)	C1–N1–C5	119.7(3)
N2–Cu1–N1	81.09(12)	C1–N1–Cu1	126.0(3)
O5–Cu1–O6	95.70(11)	C5–N1–Cu1	114.2(2)
O1–Cu1–O6	101.45(11)	C10–N2–C6	118.8(3)
N2–Cu1–O6	88.51(11)	C10–N2–Cu1	125.5(3)
N1–Cu1–O6	103.40(12)	C6–N2–Cu1	115.5(2)
C11–O1–Cu1	122.6(2)		
Complex 2			
Atoms	**Bond angle (°)**	**Atoms**	**Bond angle (°)**
O5–Co1–O5	170.27(6)	O5–Co1–N1	89.87(4)
O5–Co1–O6	87.04(4)	O6–Co1–N1	166.51(4)
O5–Co1–O6	86.90(4)	O6–Co1–N1	89.91(4)
O6–Co1–O6	102.98(6)	Co1–O6–H6OB	123.0(14)
O5–Co1–N1	97.73(4)	N1–Co1–N1	77.53(6)
Co1–O5–H5OA	118.3(13)	C5–N1–C1	118.43(11)
Co1–O5–H5OB	117.7(14)	C5–N1–Co1	126.16(9)

Co1–O6–H6OA	114.9(13)	C1–N1–Co1	115.16(9)
Complex 3			
Atoms	**Bond angle (°)**	**Atoms**	**Bond angle (°)**
O6–Zn1–O6	105.5(2)	O5–Zn1–N1	97.83(15)
O6–Zn1–O5	87.39(15)	N1–Zn1–N1	76.4(2)
O6–Zn1–O5	86.74(15)	Zn1–O6–H6OA	120(4)
O5–Zn1–O5	170.3(2)	Zn1–O6–H6OB	108(4)
O6–Zn1–N1	89.30(16)	C1–N1–C5	118.6(5)
O6–Zn1–N1	164.66(16)	C1–N1–Zn1	115.8(3)
O5–Zn1–N1	89.80(15)	C5–N1–Zn1	125.4(4)
Complex 4			
Atoms	**Bond angle (°)**	**Atoms**	**Bond angle (°)**
O5–Co1–O5	157.24(6)	O6–Co1–O6	112.72(5)
O5–Co1–N1	104.96(4)	Co1–O5–H5OA	122.2(13)
O5–Co1–N1	92.81(4)	Co1–O5–H5OB	122.1(13)
N1–Co1–N1	77.76(5)	Co1–O6–H6OA	118.2(14)
O5–Co1–O6	84.17(3)	Co1–O6–H6OB	113.9(13)
O5–Co1–O6	83.28(3)	C5–N1–C1	117.79(10)
N1–Co1–O6	85.15(4)	C5–N1–Co1	128.77(8)
N1–Co1–O6	161.27(4)	C1–N1–Co1	113.30(7)

Table S4. Simulated data for the bond length of complexes **1–4** in Angstrom (Å).

Complex 1					
Atoms	**Bond length (Å)**		**Atoms**	**Bond length (Å)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
Cu1–N1	2.016	2.066	O7–C21	1.254	1.240
Cu1–N2	1.990	2.057	O8–C21	1.246	1.263
Cu1–O1	1.954	1.962	O5–H5O(A)	0.944	0.873
Cu1–O5	1.950	1.999	O6–H6O(B)	0.929	1.064
Cu1–O6	2.261	2.199	O6–H6O(A)	0.931	0.970
O1–C11	1.281	1.284	O5–H5O(B)	0.930	0.875
O2–C11	1.225	1.227			
Complex 2					
Atoms	**Bond length (Å)**		**Atoms**	**Bond length (Å)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
Co1–N1	2.1380	1.889	O1–C6	1.2362	1.241
Co1–O5	2.0606	2.046	O2–C6	1.2807	1.243
Co1–O6	2.1227	2.315			
Complex 3					
Atoms	**Bond length (Å)**		**Atoms**	**Bond length (Å)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
Zn1–O6	2.117	2.211	O1–C6	1.290	1.296
Zn1–O5	2.125	2.069	O2–C6	1.227	1.214
Zn1–N1	2.157	2.130			

Complex 4					
Atoms	**Bond length (Å)**		**Atoms**	**Bond length (Å)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
Co1–O5	2.0228	2.0228	O1–C7	1.2342	1.2341
Co1–N1	2.1632	2.1631	O2–C7	1.2809	1.2808
Co1–O6	2.1634	2.1632			

Table S5. Simulated data for the bond angles of complexes **1**–**4** in degree (°).

Complex 1					
Atoms	**Bond angle (°)**		**Atoms**	**Bond angle (°)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
O5–Cu1–O1	89.65	88.51	Cu1–O5–H5OA	119	118.21
O5–Cu1–N2	173.65	173.71	Cu1–O5–H5OB	109	109.47
O1–Cu1–N2	94.18	94.80	Cu1–O6–H6OA	90	90.47
O5–Cu1–N1	93.28	93.71	Cu1–O6–H6OB	113	113.83
O1–Cu1–N1	154.55	155.71	C1–N1–C5	119.7	119.97
N2–Cu1–N1	81.09	79.58	C1–N1–Cu1	126.0	125.57
O5–Cu1–O6	95.70	99.85	C5–N1–Cu1	114.2	114.32
O1–Cu1–O6	101.45	101.72	C10–N2–C6	118.8	120.25
N2–Cu1–O6	88.51	88.51	C10–N2–Cu1	125.5	124.74
N1–Cu1–O6	103.40	102.57	C6–N2–Cu1	115.5	114.63
C11–O1–Cu1	122.6	123.99			
Complex 2					
Atoms	**Bond angle (°)**		**Atoms**	**Bond angle (°)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
O5–Co1–O5	170.27	170.20	N1–Co1–N1	77.53	75.40
O5–Co1–O6	87.04	87.65	Co1–O5–H5OA	118.3	119.47
O5–Co1–O6	86.90	88.42	Co1–O5–H5OB	117.7	118.05
O6–Co1–O6	102.98	101.13	Co1–O6–H6OA	114.9	114.97
O5–Co1–N1	89.87	90.19	Co1–O6–H6OB	123.0	120.75
O5–Co1–N1	97.73	98.10	C5–N1–C1	118.43	117.62
O6–Co1–N1	89.92	89.02	C5–N1–Co1	126.16	126.75
O6–Co1–N1	166.50	166.99	C1–N1–Co1	115.16	114.52
Complex 3					
Atoms	**Bond angle (°)**		**Atoms**	**Bond angle (°)**	
	Exp.	**Obs.**		**Exp.**	**Obs.**
O6–Zn1–O6	105.5	104.47	O5–Zn1–N1	89.80	89.86
O6–Zn1–O5	87.39	87.28	N1–Zn1–N1	76.4	79.06
O6–Zn1–O5	86.74	87.09	Zn1–O6–H6OA	120	120.27
O5–Zn1–O5	170.3	169.22	Zn1–O6–H6OB	108	109.47
O6–Zn1–N1	164.66	164.18	C1–N1–C5	118.6	119.24
O6–Zn1–N1	89.30	90.93	C1–N1–Zn1	115.8	112.99
O5–Zn1–N1	97.83	96.01	C5–N1–Zn1	125.4(4)	127.52
Complex 4					
Atoms	**Bond angle (°)**		**Atoms**	**Bond angle (°)**	

	Exp.	Obs.		Exp.	Obs.
O5–Co1–O5	157.24	158.75	O6–Co1–O6	112.72	112.72
O5–Co1–N1	104.96	105.37	Co1–O5–H5OA	122.2	121.67
O5–Co1–N1	92.81	92.80	Co1–O5–H5OB	122.1	121.17
N1–Co1–N1	77.76	78.02	Co1–O6–H6OA	118.2	118.82
O5–Co1–O6	84.17	84.17	Co1–O6–H6OB	113.9	113.45
O5–Co1–O6	83.28	83.27	C5–N1–C1	117.79	117.79
N1–Co1–O6	85.15	85.14	C5–N1–Co1	128.77	128.76
N1–Co1–O6	161.27	161.26	C1–N1–Co1	113.30	113.29

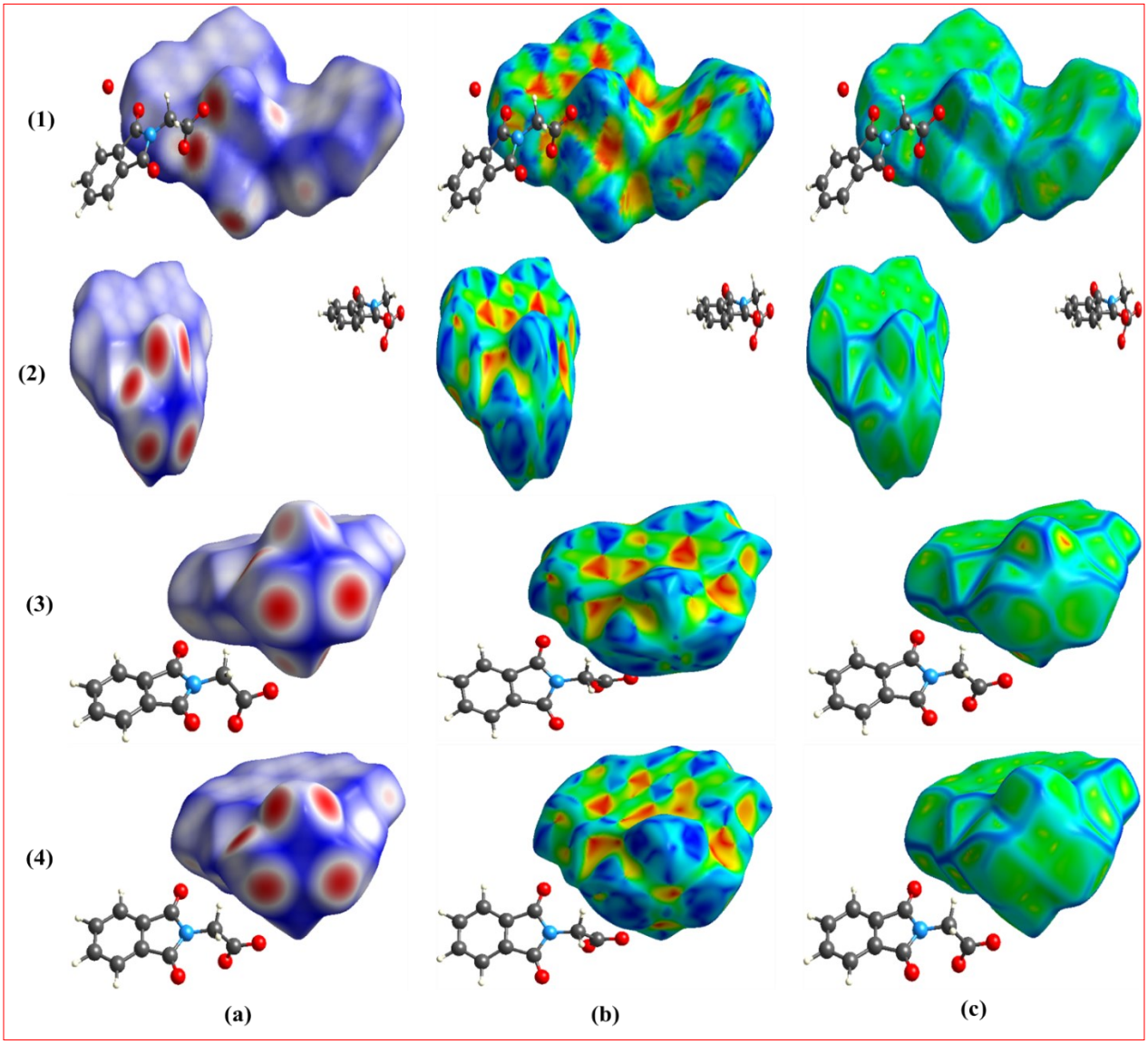


Fig. S7. Hirshfield surface for complexes **1**–**4** (a) d_{norm} (b) shape index and (c) curvedness.

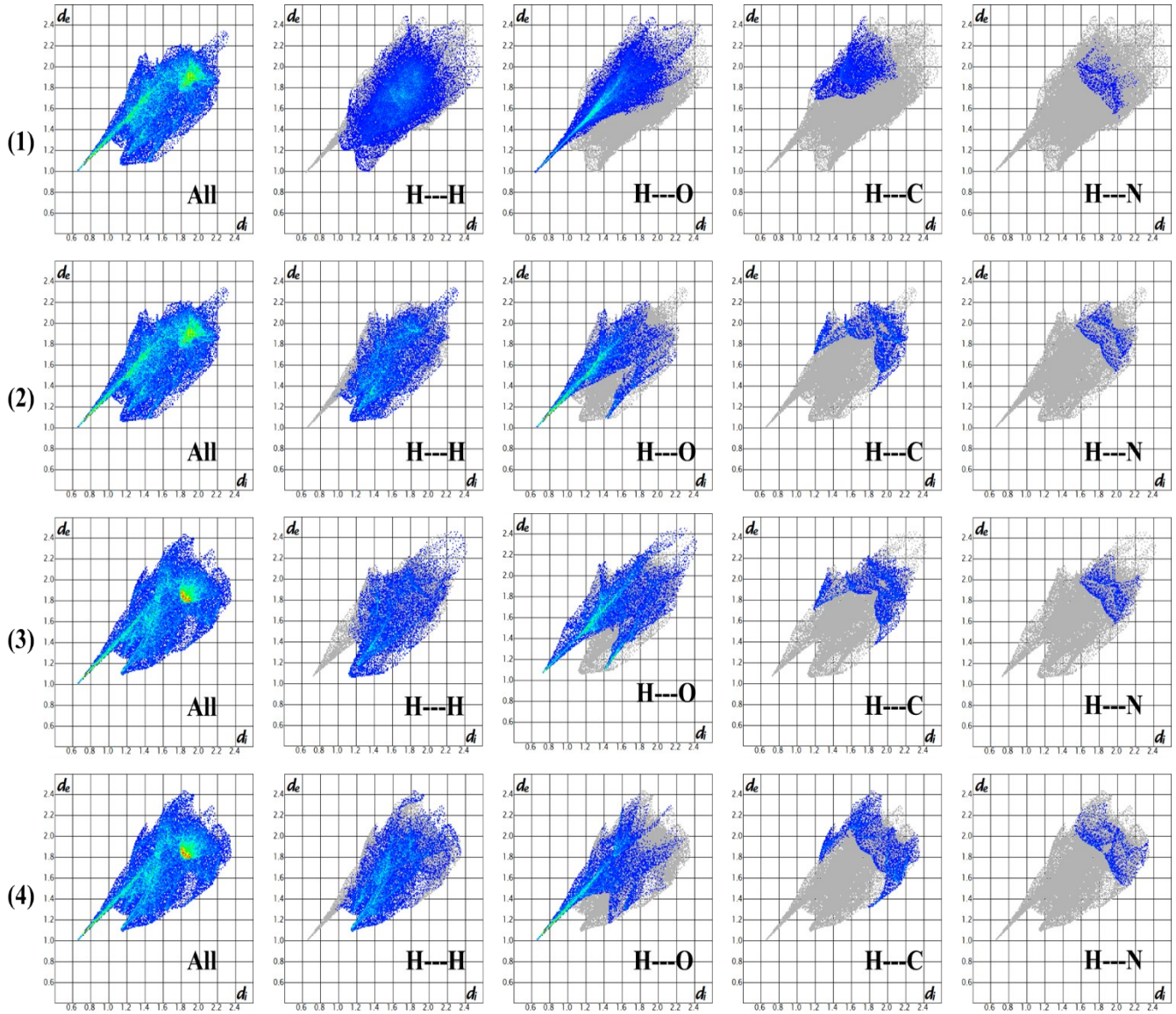


Fig. S8. Finger print plots for complexes **1**–**4** discerning the percent contribution by various inter-atomic interactions.

Table S6. Percentage contribution of various atomic pairs in the complexes **1**–**4**.

	Percent contribution (%)			
Complexes	**H–H**	**H–O**	**H–C**	**H–N**
1	32.1	37.4	11.3	1.2
2	33.6	41.3	9.1	2.7
3	28.0	39.0	9.1	3.0
4	40.7	29.9	10.4	3.7

Binding studies with ct–DNA and tRNA

Absorption titrations were performed on a UV–1700 PharmaSpec UV–vis spectrophotometer (Shimadzu) with a fixed concentration of complexes **1–4** ($1x10^{-4}$ M) and varying the ct–DNA/tRNA (0–0.55 $x10^{-5}$ M) concentration while the total volume remains constant. The absorbance was recorded after successive titrations upon addition of ct–DNA/tRNA solution. Fluorescent Intercalator Displacement assay was performed using a Hitachi F–250 spectro–fluorometer at 25 °C. The Tris buffer was used as a blank to make preliminary adjustments. Emission spectral titrations were conducted by adding aliquots of 0–0.6 $x10^{-4}$ M solutions of complexes **1–4** to samples containing 1μM of ethidium bromide solution ($1x10^{-5}$ M) and an equimolar concentration of ct–DNA/tRNA (1 $x10^{-5}$ M) in Tris–HCl buffer. Cyclic voltammetry was carried out at CH instrument electrochemical analyzer. The cyclic voltammograms were recorded for the complexes alone and then in the absence and presence of ct–DNA and tRNA (1 $x10^{-5}$ M). The total volume of the solution is maintained constant by the addition of Tris–HCl buffer.

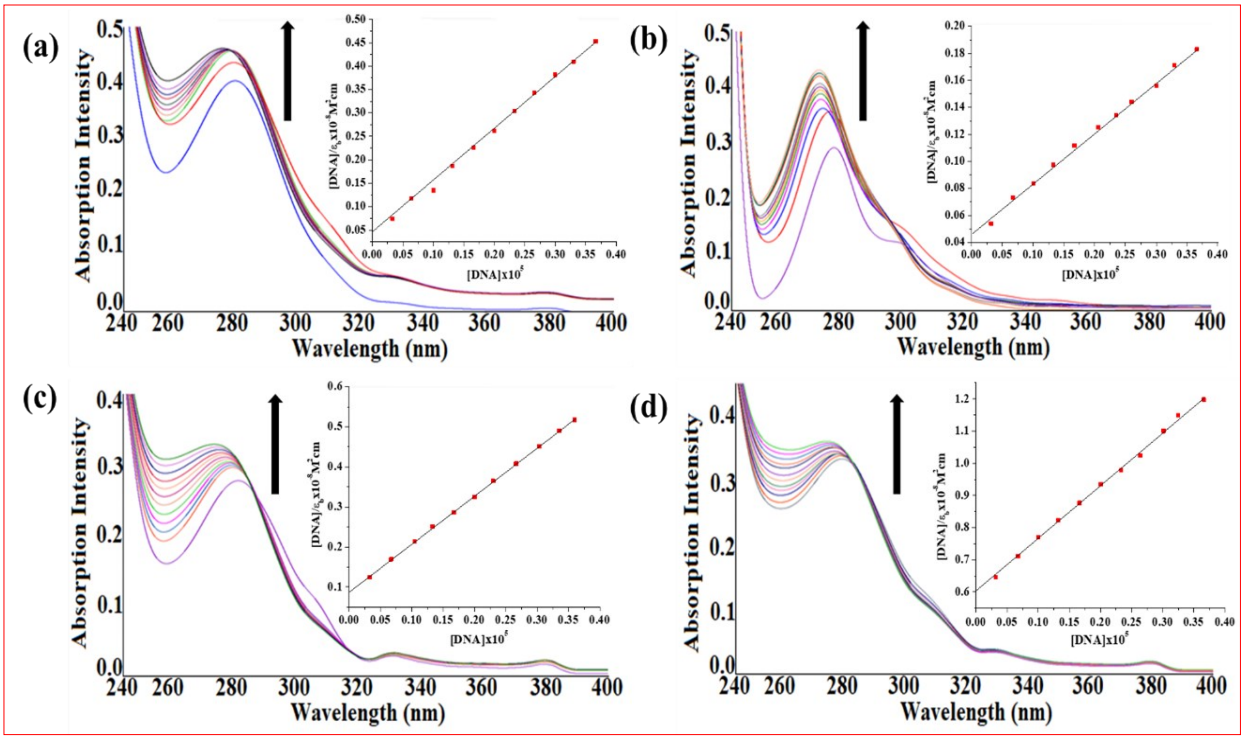


Fig. S9. Absorption spectra of complexes **1–4** in presence of increasing ct–DNA concentration (0–0.55 x10^{-5} M).

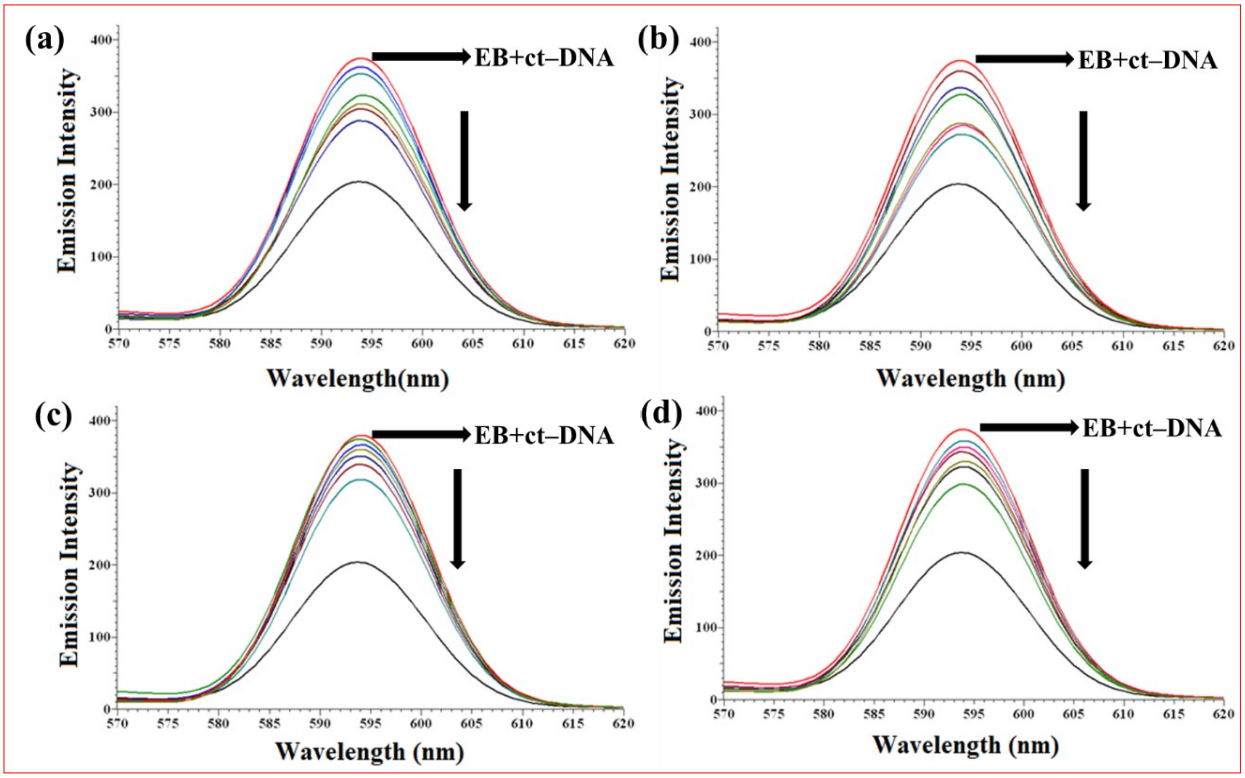


Fig. S10. Emission titration spectra of EB–ct–DNA system in presence of increasing concentration of complexes **1–4**.

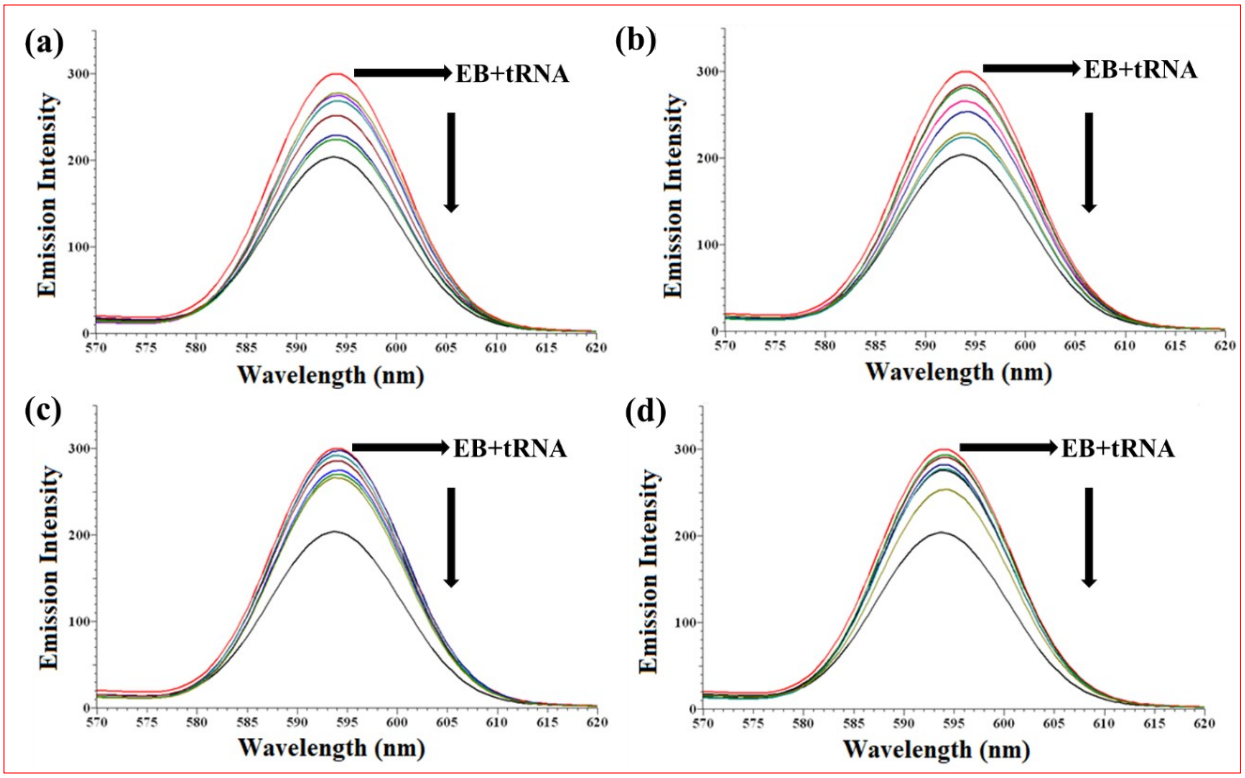


Fig. S11. Emission titration spectra of EB–tRNA system in presence of increasing concentration of complexes **1**–**4**.

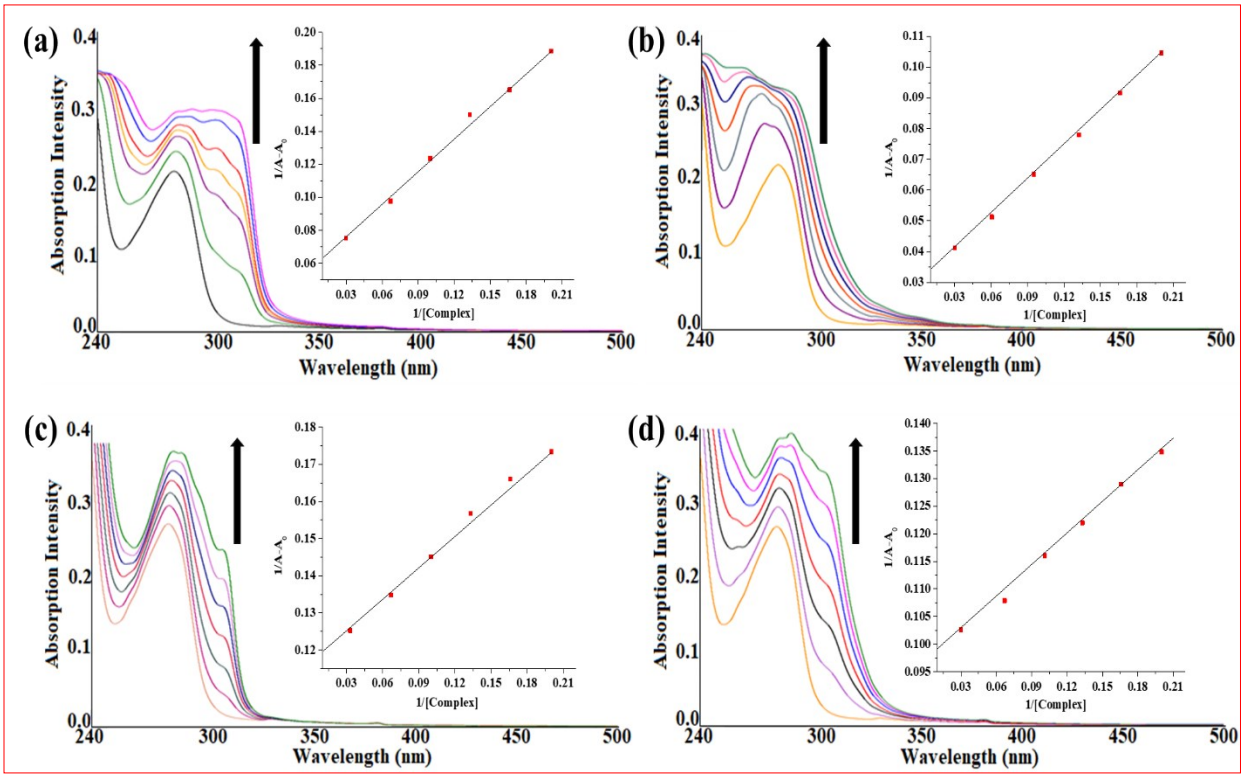


Fig. S12. Absorption titration spectra of BSA in presence of increasing amount of complexes **1**–**4**.

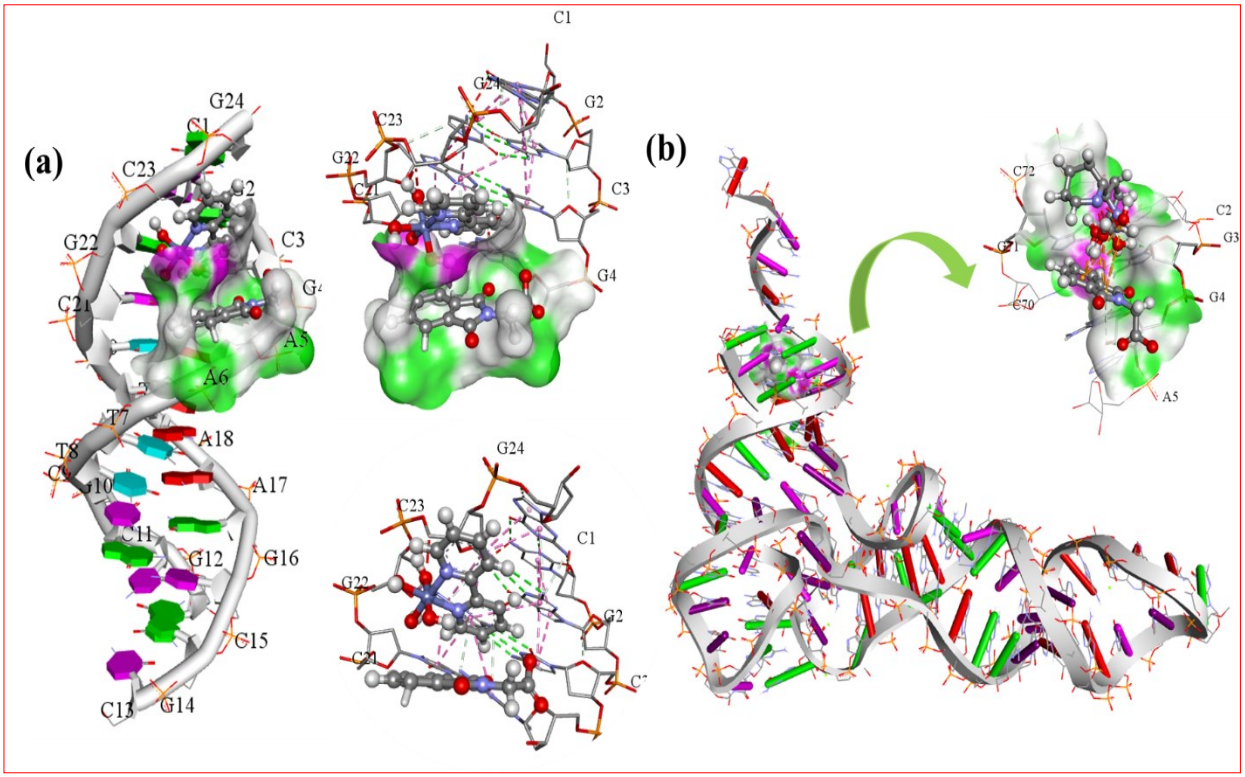


Fig. S13. Molecular docked model of complex **2** with (a) DNA and (b) RNA.

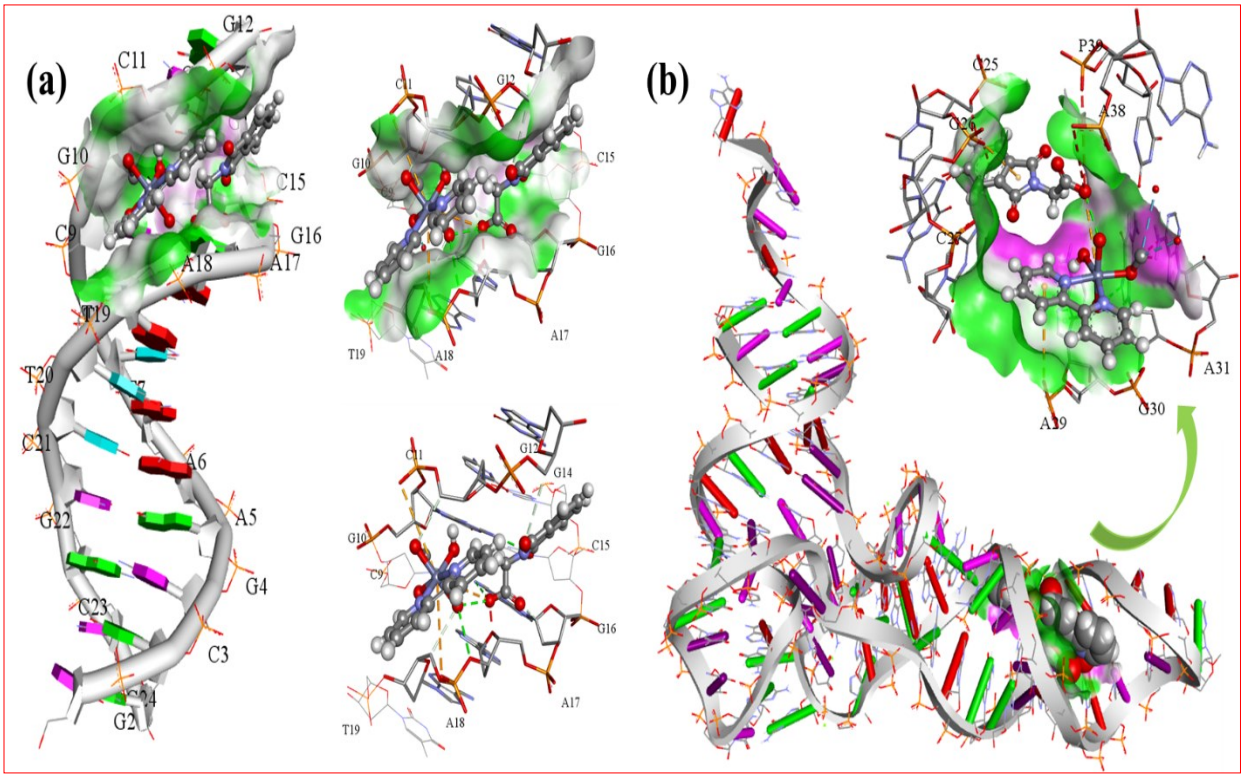


Fig. S14. Molecular docked model of complex **3** with (a) DNA and (b) RNA.

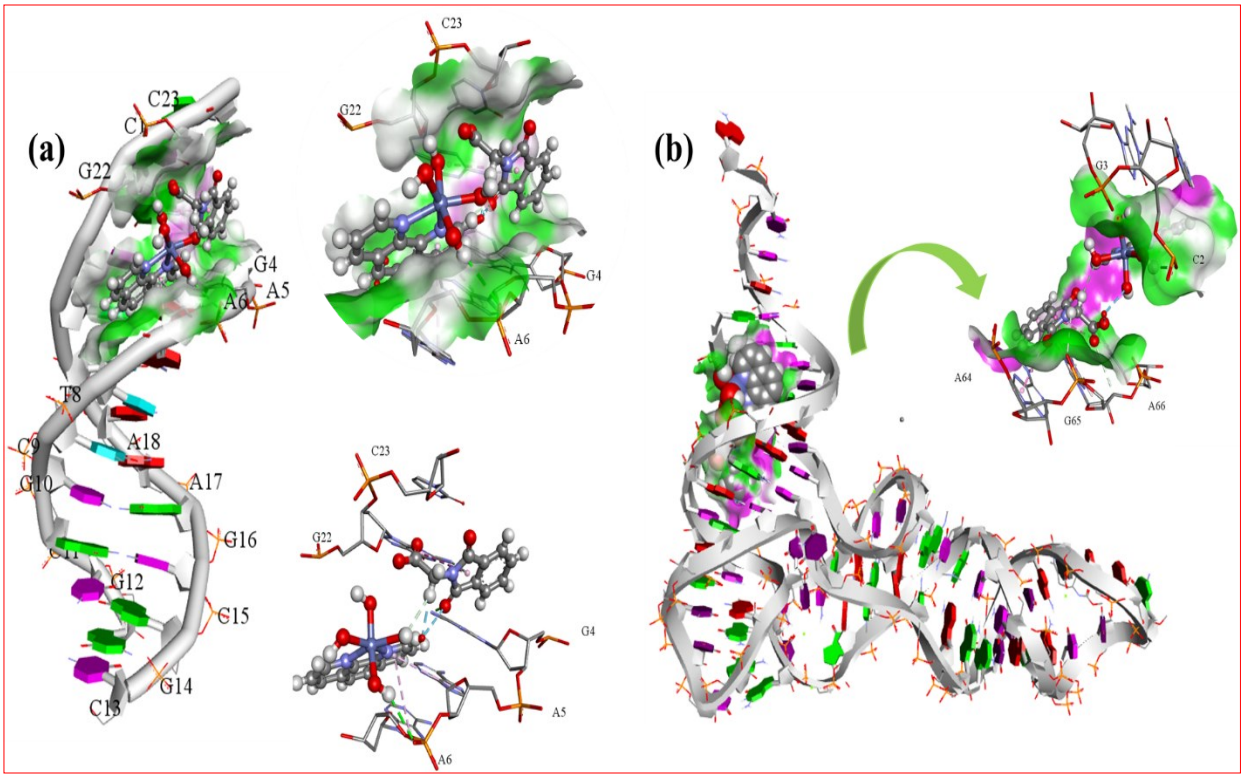


Fig. S15. Molecular docked model of complex **4** with (a) DNA and (b) RNA.