Supplementary Information

Synthesis, characterization, theoretical study and molecular docking studies of some new cobalt(II), chromium(II) and nickel (II) complexes

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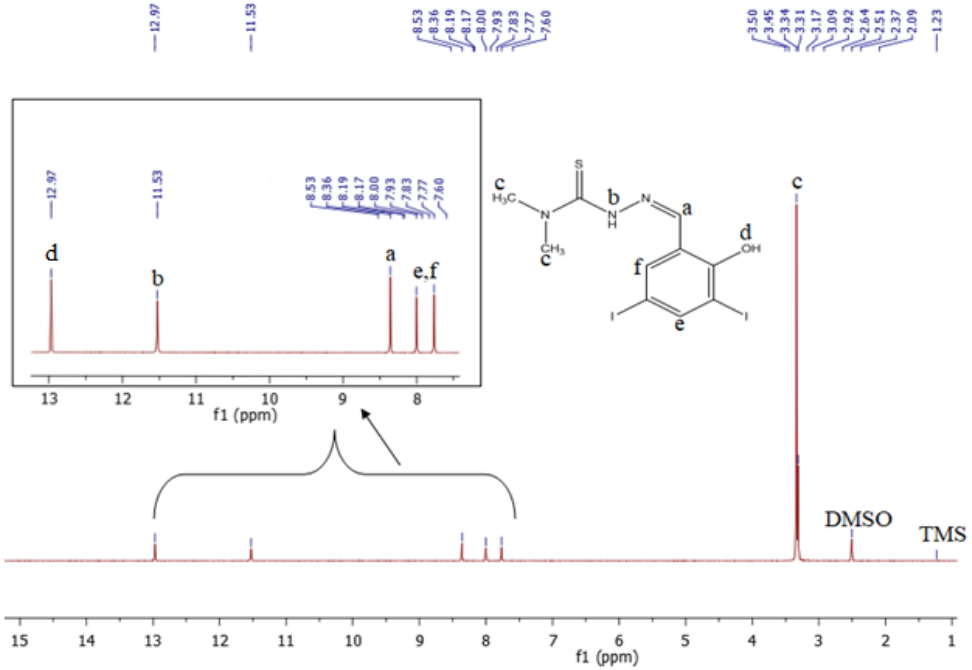

Figure S1 — ^{1}H-NMR spectrum of the ligand (**HL**)

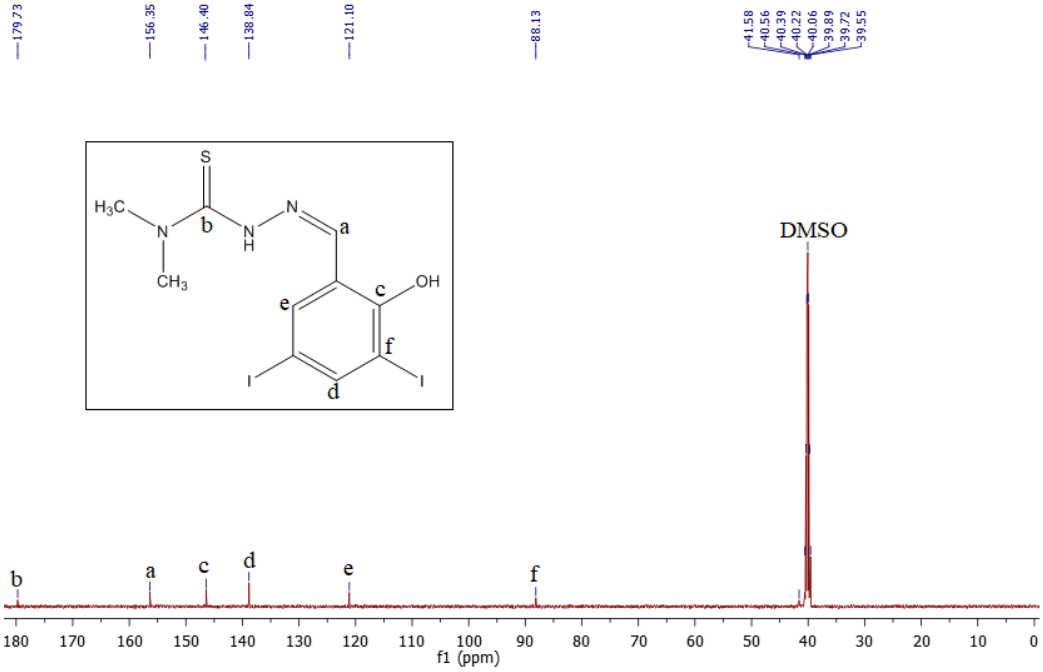

Figure S2 — 13C-NMR spectrum of the ligand (**HL**)

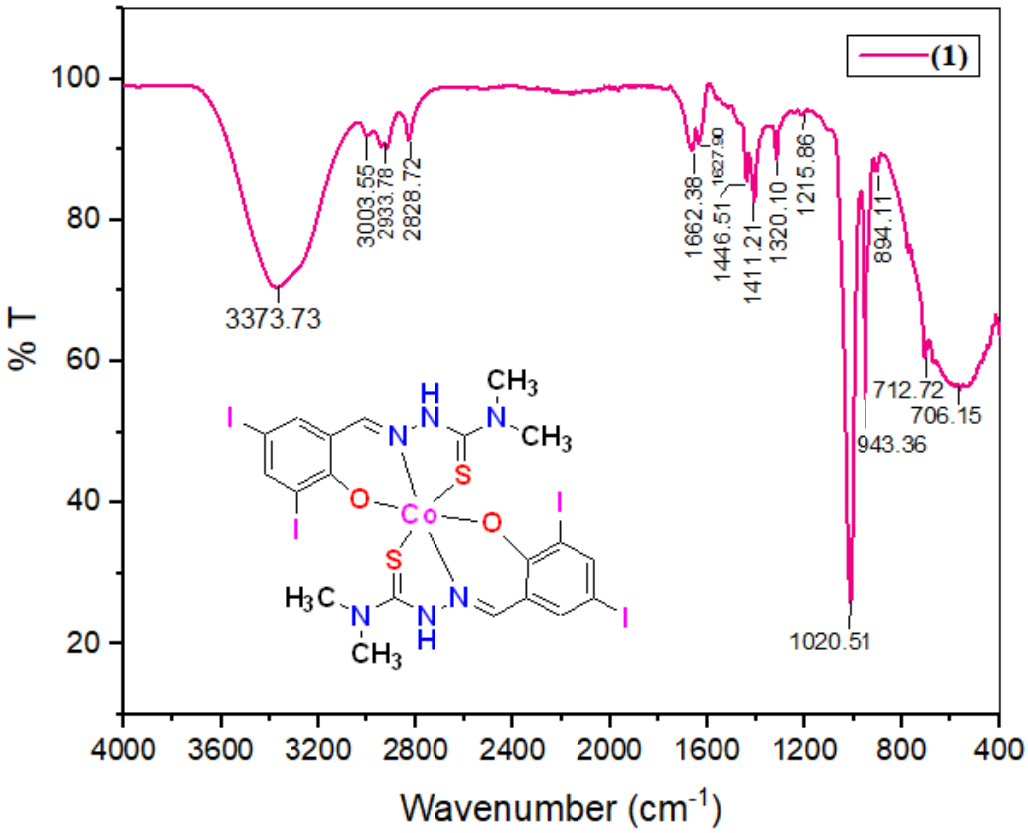

Figure S3 — Infrared spectra of the cobalt(II) complex (**1**)

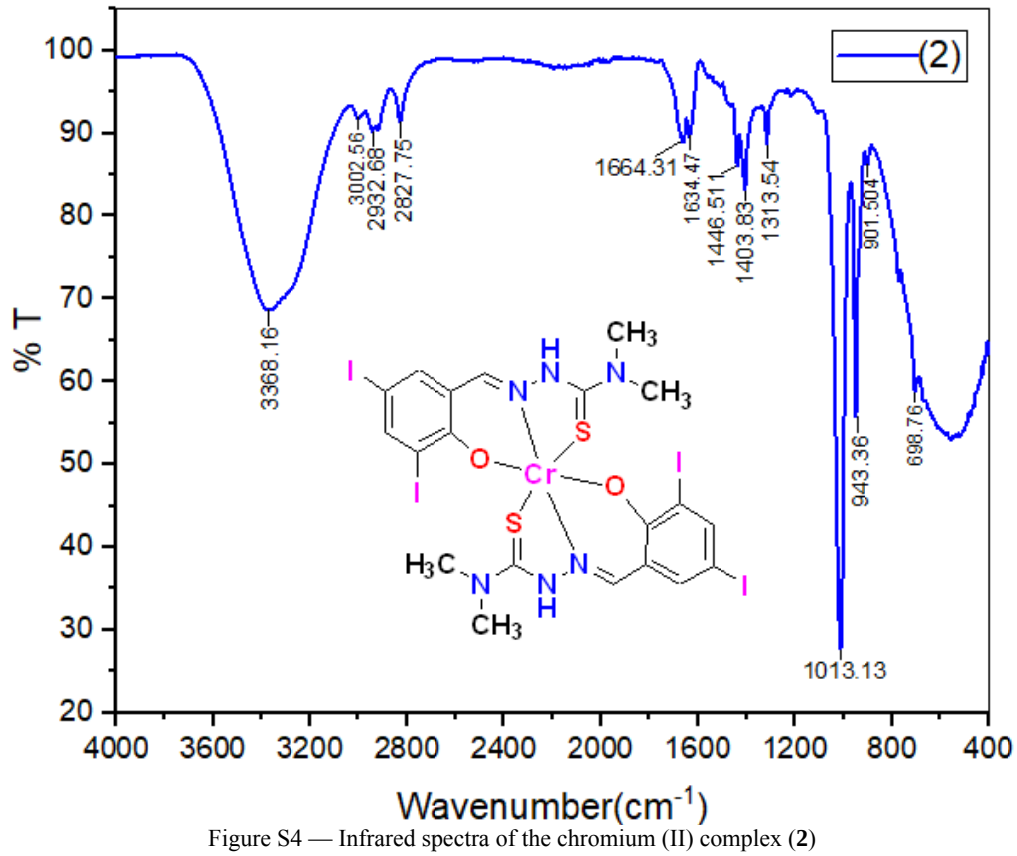

Figure S4 — Infrared spectra of the chromium (II) complex (**2**)

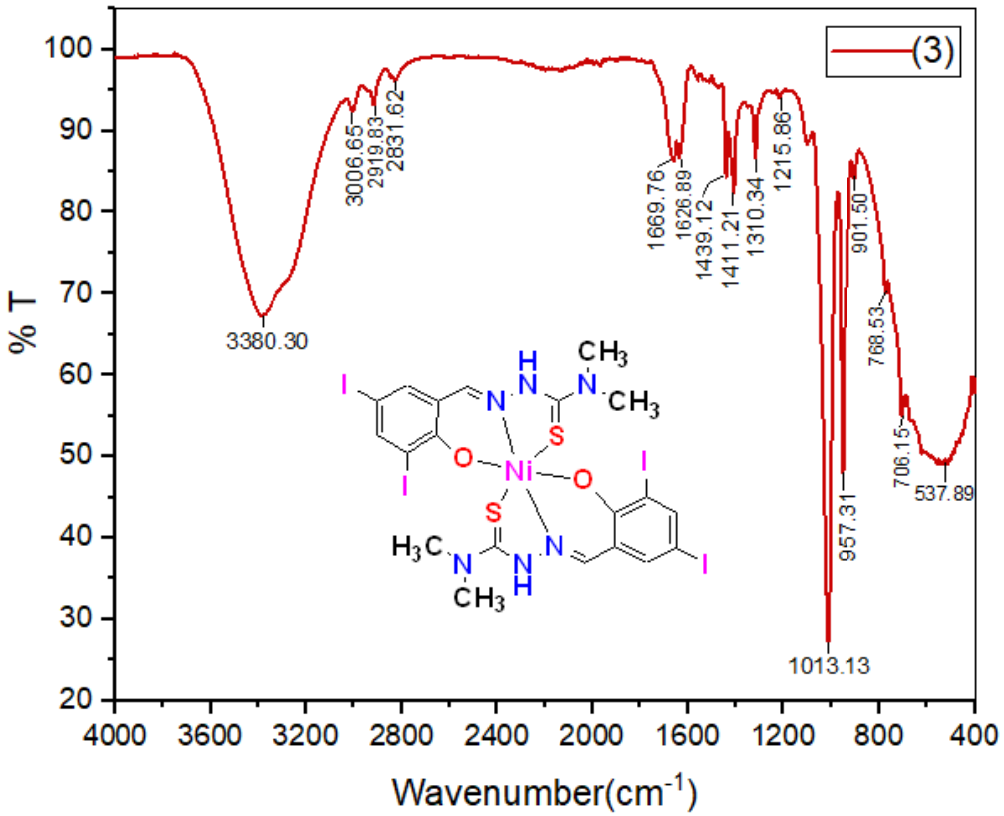

Figure S5 — Infrared spectra of the nickel(II) complex (**3**)

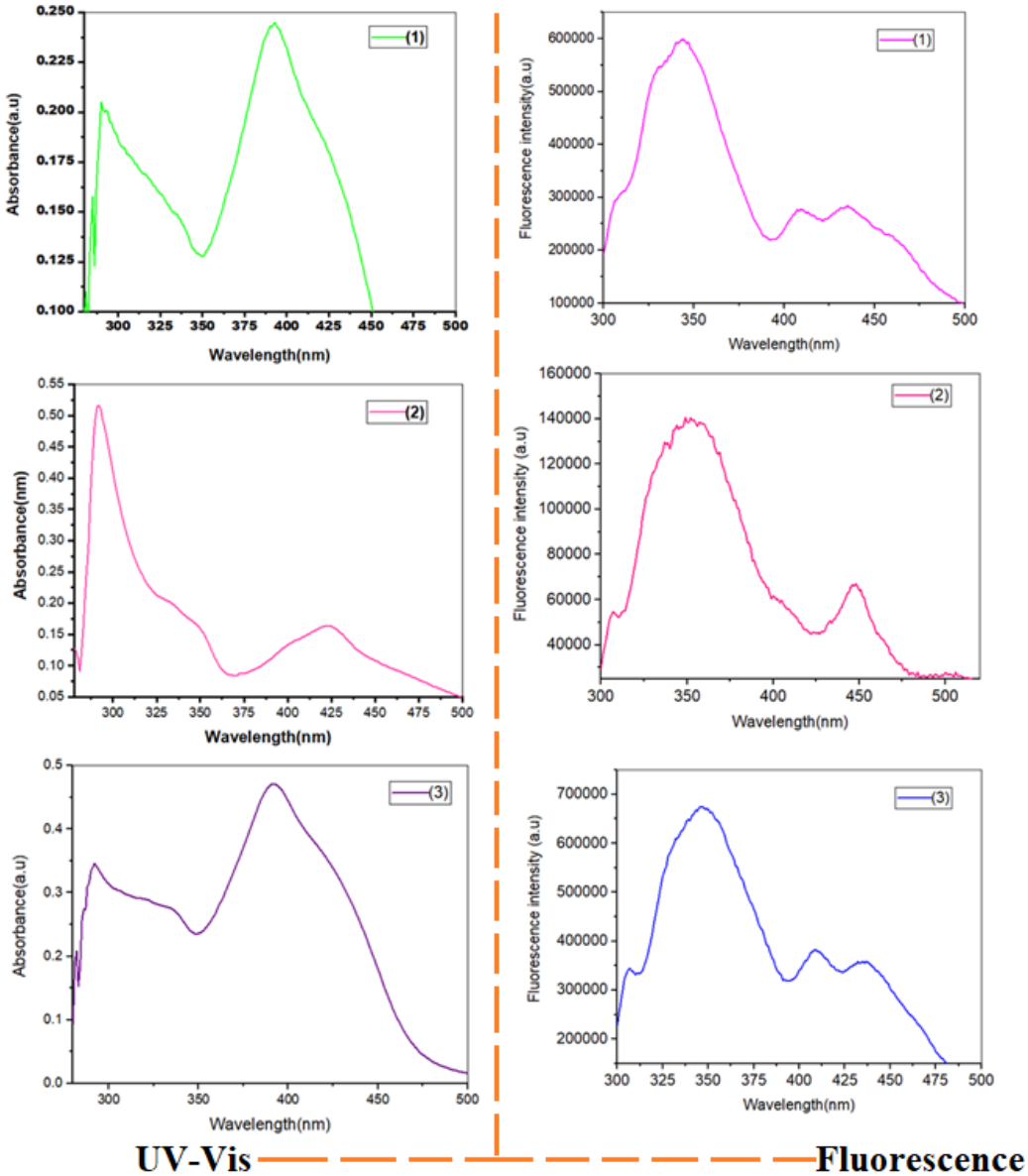

Figure S6 — UV-Vis and fluorescence spectra (1×10^{-5} M) for metal(II) complexes (**1**)-(**3**)

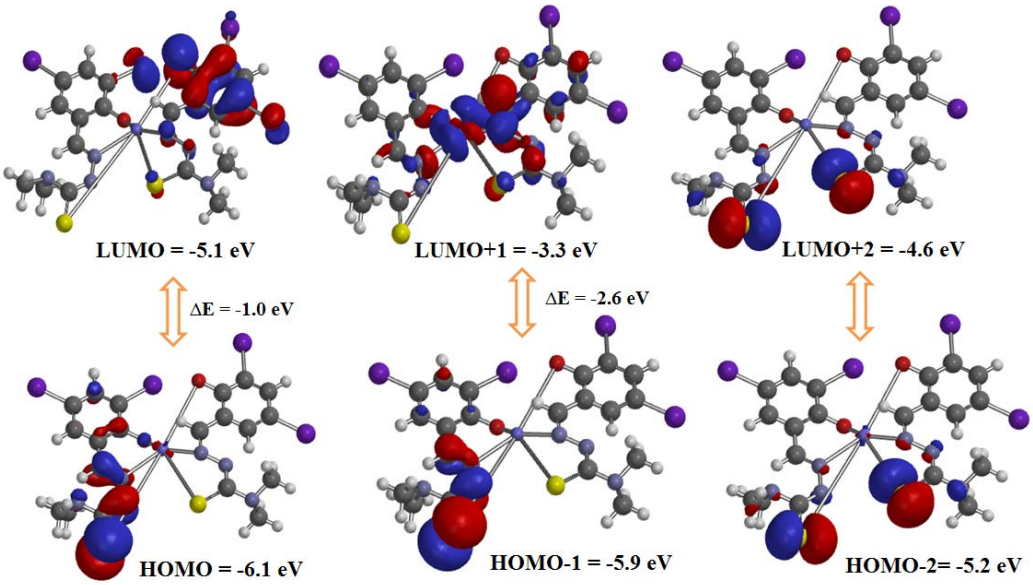

Figure S7 — Frontier molecular orbitals of the studied cobalt (II) complex (**1**)

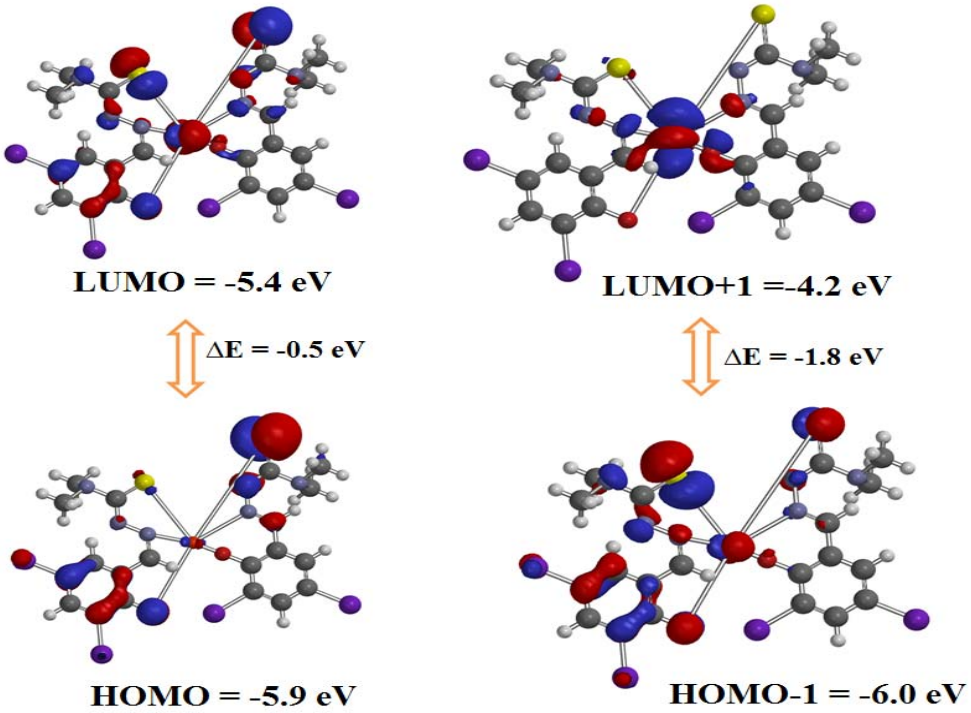

Figure S8 — Frontier molecular orbitals of the studied chromium (II) complex (**2**)

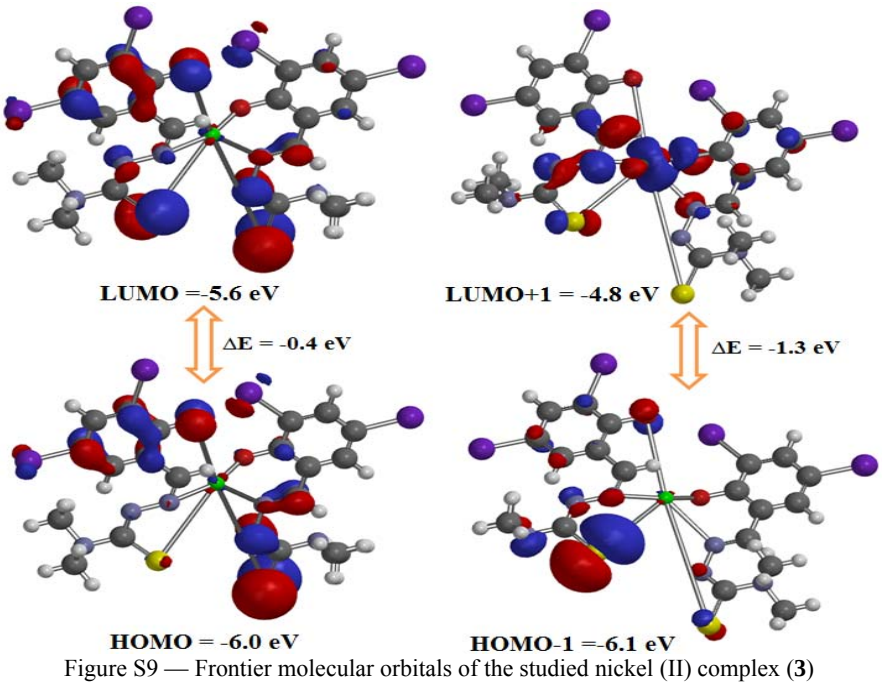

Figure S9 — Frontier molecular orbitals of the studied nickel (II) complex (**3**)

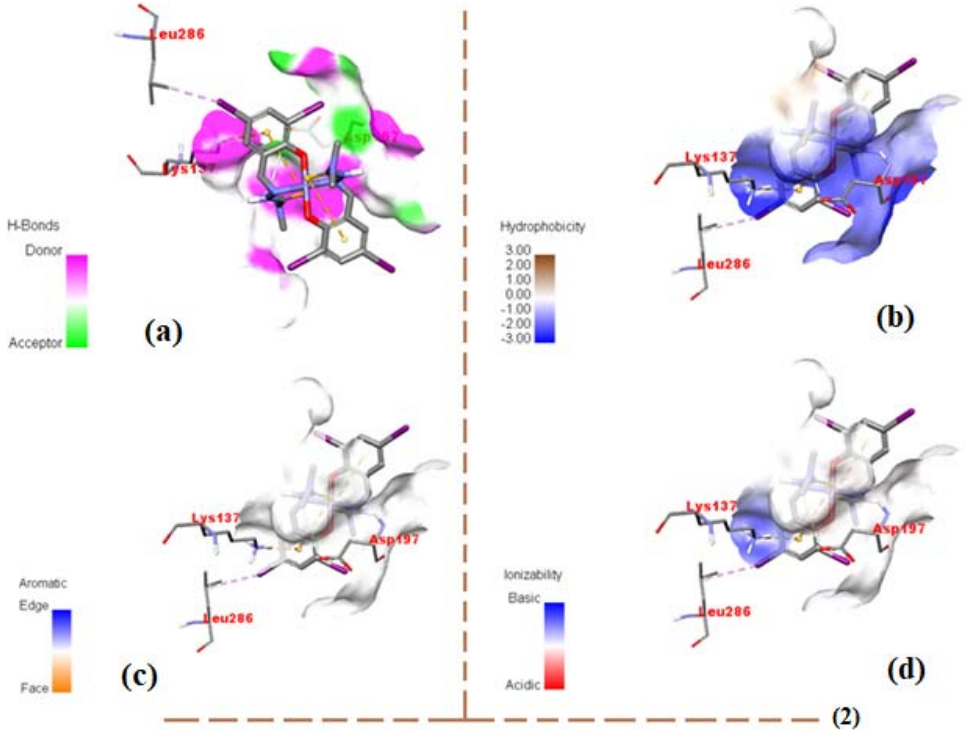

Figure S10 — Receptor surface of docked conformations for Schiff base chromium(II) complex (**2**) inside the M^{pro} with its focused view for interacting residues (PDB ID: 7JKV) with H bond and intermolecular interactions; (a) H-bond donor and acceptor meshes represented by pink and light green colors, respectively; (b) hydrophobic pocket represented with blue and brown colors;(c) Aromatic receptor surface represented by blue(Edge) and orange (face) colors; (d) Ionizability receptor surface represented by blue and red colors, respectively

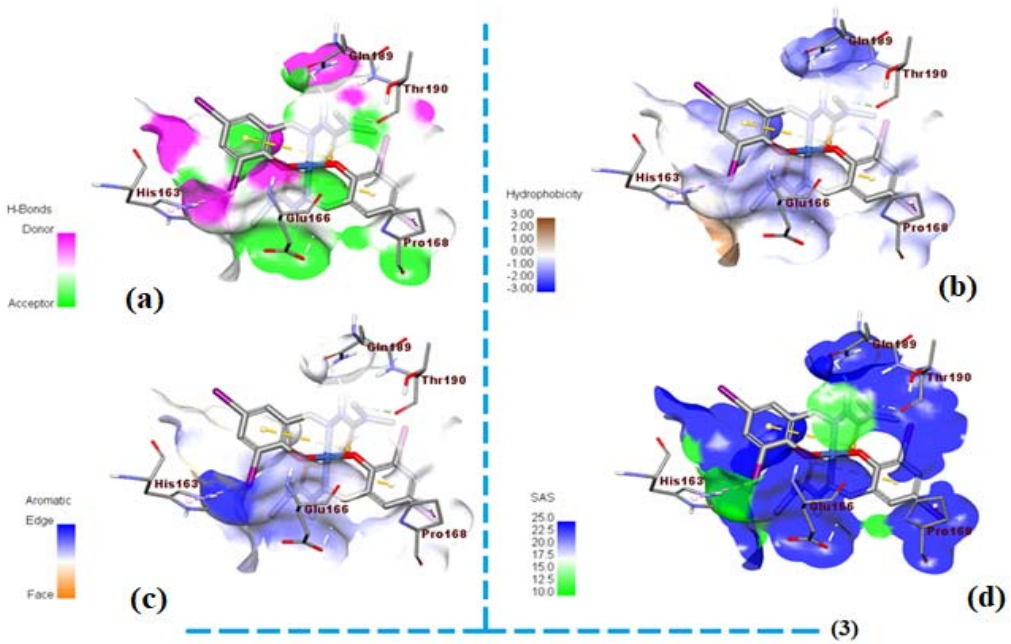

Figure S11 — Receptor surface of docked conformations for Schiff base nickel(II) complex (**3**) inside the M^{pro} with its focused view for interacting residues (PDB ID: 7JKV) with H bond and intermolecular interactions; (a) H-bond donor and acceptor meshes represented by pink and light green colors, respectively; (b) hydrophobic pocket represented with blue and brown colors;(c) Aromatic receptor surface represented by blue(Edge) and orange (face) colors; (d) SAS receptor surface represented by sky blue and light green colors, respectively

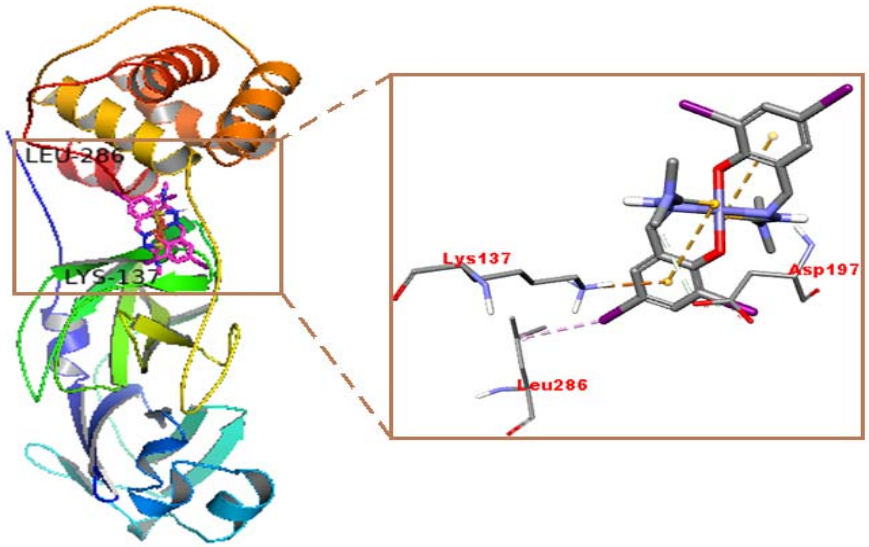

Figure S12 — The docked Schiff base chromium (II) complex (**2**) inside the M^{pro} (PDB ID: 7JKV) with its focused view for interacting residues around the docked ligand

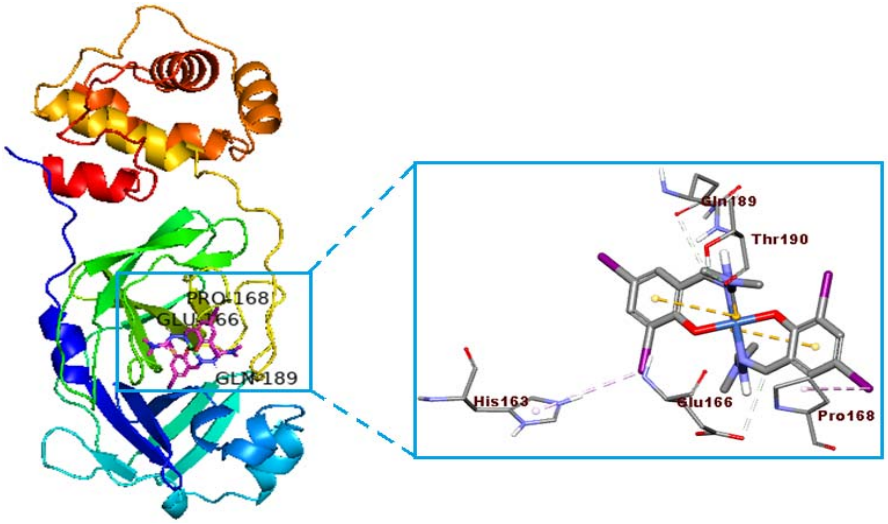

Figure S13 — The docked Schiff base nickel (II) complex (**3**) inside the M^{pro} (PDB ID: 7JKV) with its focused view for interacting residues around the docked ligand

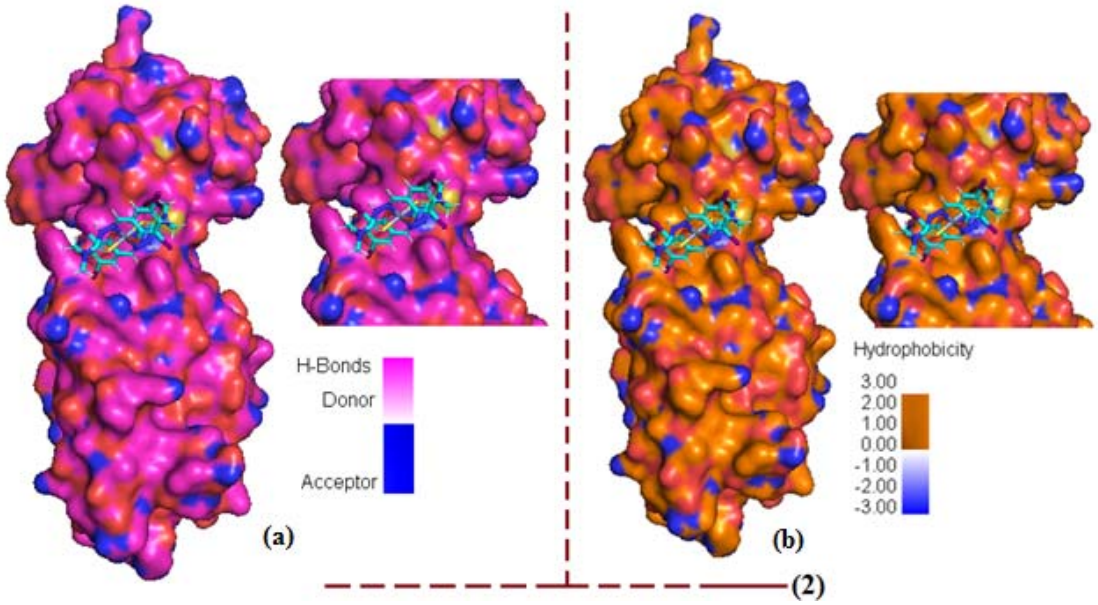

Figure S14 — The total density surfaces representation for docked Schiff base chromium(II) complex (**2**) inside the M^{pro} (PDB ID: 7JKV) (a) with hydrogen bond donor and acceptor meshes represented by pink and blue colors, respectively (b) Surface representation of hydrophobic pocket represented with deep orange and sky blue colors

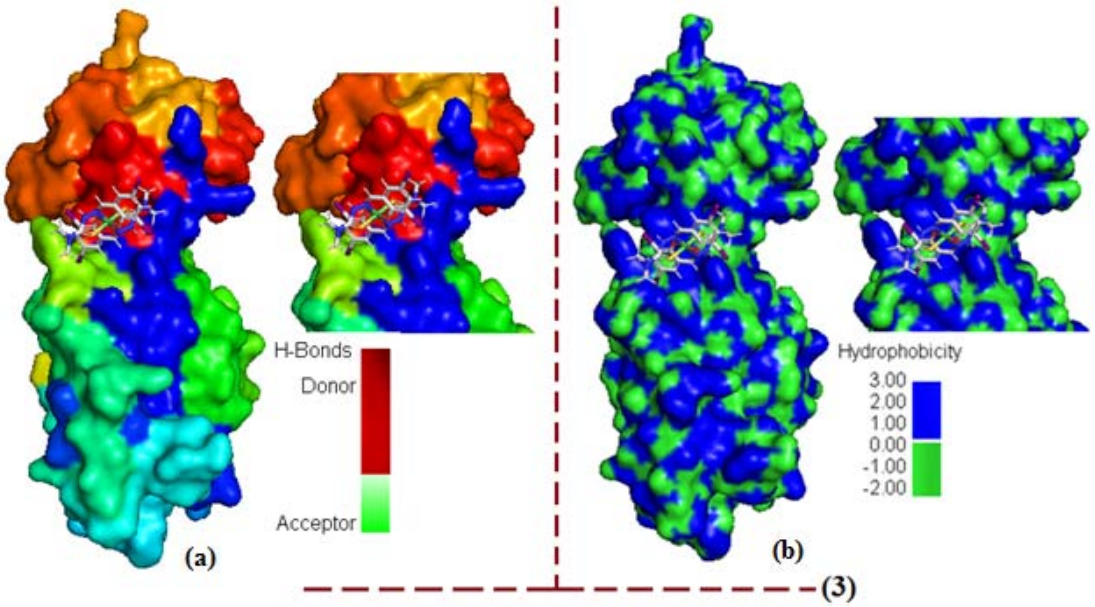

Figure S15 — The total density surfaces representation for docked Schiff base nickel(II) complex (**3**) inside the M^{pro} (PDB ID: 7JKV) (a) with hydrogen bond donor and acceptor meshes represented by deep red and light green colors, respectively (b) Surface representation of hydrophobic pocket represented with light green and blue colors

Table S1 — The computed values of E_{HOMO}, E_{LUMO} and energy gap (E_{LUMO}-E_{HOMO})[a] studied complexes (**1**)-(**3**)									
Complexes	E_{HOMO}	E_{LUMO}	ΔE	E_{HOMO-1}	E_{LUMO+1}	ΔE	E_{HOMO-2}	E_{LUMO+2}	ΔE
(**1**)	-6.1	-5.1	1.0	-5.9	-3.3	2.6	-5.2	-4.6	0.6
(**2**)	-5.9	-5.4	0.5	-6.0	-4.2	1.8	-4.9	-3.5	1.4
(**3**)	-6.0	-5.6	0.4	-6.1	-4.8	1.3	-6.2	-5.8	0.4

[a] Energy gap (ΔE) = E_{LUMO}-E_{HOMO}, units in eV

Table S2 — Computed values for Global reactivity descriptors of the studied complexes (**1**)-(**3**)							
Complexes	*IP*	*EA*	χ	η	μ	ω	ω
(**1**)	6.1	5.1	5.6	0.5	-5.6	31.4	1.0
(**2**)	5.9	5.4	5.7	0.3	-5.7	54.2	1.7
(**3**)	6.0	5.6	5.8	0.2	-5.8	84.1	2.5

IP = ionization potential, *EA* = electron affinity, χ = electro negativity, μ = chemical potential, η = global hardness, σ=global softness and ω = global electrophilicity; units in *eV*

Table S3 — Pharmacokinetic properties of the new metal complexes (**1**)-(**3**)				
Property	Model Name	Predicted Value		
		(**1**)	(**2**)	(**3**)
Absorption	Water solubility(log mol/L)	-4.302	-4.304	-4.403
	$Caco_2$ permeability(log Papp in 10^{-6} cm/s)	0.977	1.032	1.625
	Intestinal absorption (human) (%Absorbed)	94.819	96.381	96.281
	Skin Permeability(Log Kp)	-2.735	-2.705	-2.805
	P-glycoprotein Substrate	No	No	No
	P-glycoprotein I inhibitor	Yes	Yes	Yes
	P-glycoprotein II inhibitor	Yes	Yes	Yes
Distribution	VDss (human) (log L/kg)	-0.635	0.607	0.627
	Fraction unbound (human) (Fu)	0.388	0.391	0.398
	BBB permeability(log BB)	-1.034	-1.371	-1.398
	CNS permeability(log PS)	-1.629	-1.433	-1.698
Metabolism	CYP2D6 substrate	No	No	No
	CYP3A4 substrate	No	No	No
	CYP1A2 substrate	No	No	No
	CYP2C19 inhibitor	No	No	No
	CYP2C9 inhibitor	No	No	No

	CYP2D6 inhibitor	No	No	No
	CYP3A4 inhibitor	No	No	No
Excretion	Total Clearance (log ml/min/kg)	-0.736	-0.697	-0.869
	Renal OCT2 substrate	No	No	No
Toxicity	AMES toxicity	No	No	No
	Max. tolerated dose (human) (log mg/kg/day)	1.439	1.351	2.321
	hERG I inhibitor	No	No	No
	hERG II inhibitor	Yes	Yes	Yes
	Oral Rat Acute Toxicity (LD50) (mol/kg)	2.626	3.072	4.207
	Oral Rat Chronic Toxicity (LOAEL) (log mg/kg bw/day)	-1.758	1.065	2.036
	Hepatotoxicity	Yes	Yes	Yes
	Skin Sensation	No	No	No
	T. Pyriformis toxicity(log ug/L)	1.285	1.332	1.521
	Minnow toxicity(log Mm)	-8.469	-6.184	-8.365

Table S4 — Chemoinformatics properties of the new metal complexes (**1**)-(**3**)

Model Name	Predicted Value		
	(**1**)	(**2**)	(**3**)
Molecular Formula	$C_{20}H_{20}CoI_4N_6O_2S_2$	$C_{20}H_{20}CrI_4N_6O_2S_2$	$C_{20}H_{20}NiI_4N_6O_2S_2$
Molecular Weight (g/mol)	1007.10	1000.17	1006.86
GPCR ligand	-0.83	-0.17	-0.17
Ion channel modulator	-1.69	-0.27	-0.28
Kinase inhibitor	-1.22	-0.15	-0.15
Nuclear receptor ligand	-1.29	-0.19	-0.18
Protease inhibitor	-0.61	-0.25	-0.25
Enzyme inhibitor	-1.17	-0.13	-0.12
miLogP	6.88	6.87	6.86
TPSA	60.88	60.87	137.90
natoms	35	35	35
nON	8	8	8
nOHNH	2	2	2
nviolations	2	2	2
nrotb	2	2	2
volume	504.09	504.05	505.10
LogP	6.68942	6.67548	6.57451
Rotatable Bonds	2	2	2
Acceptors	2	2	2
Donors	2	2	2
Surface area	324.627	325.128	324.214