Supporting Information

Synthesis, Characterization, and Biological Applications of Zinc(II) Complexes of Methylthiosalicylate Ligand

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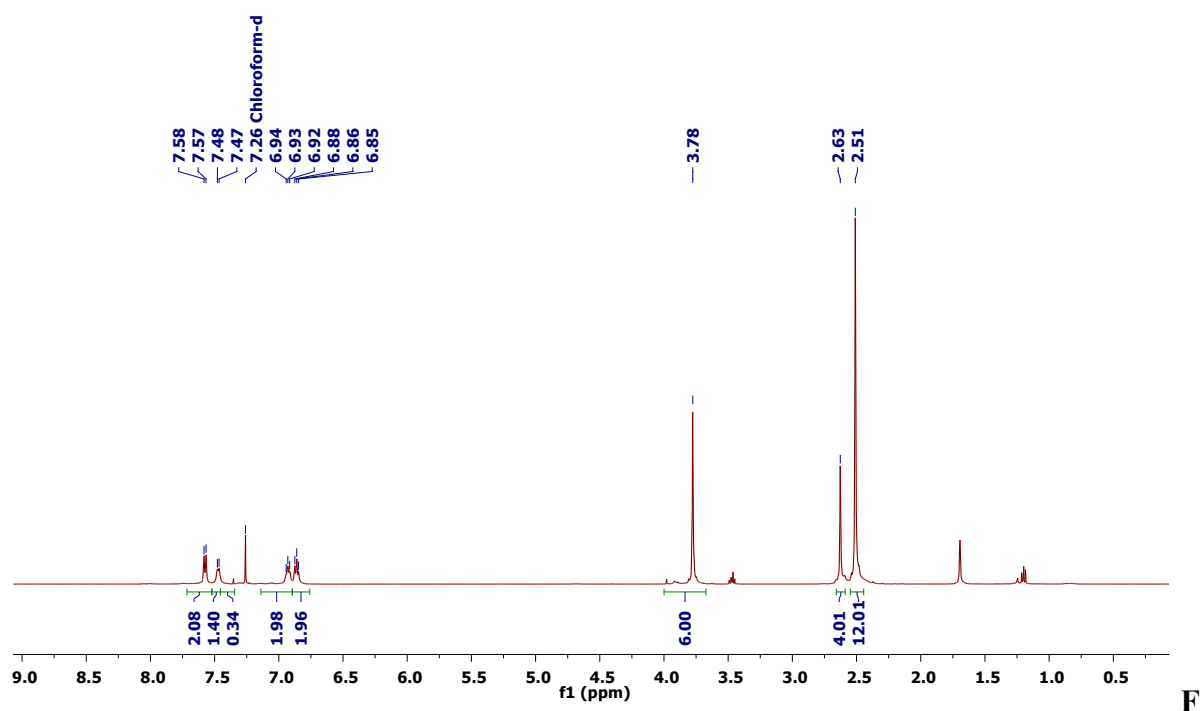
igure S1- ^{1}H NMR spectrum of complex 1
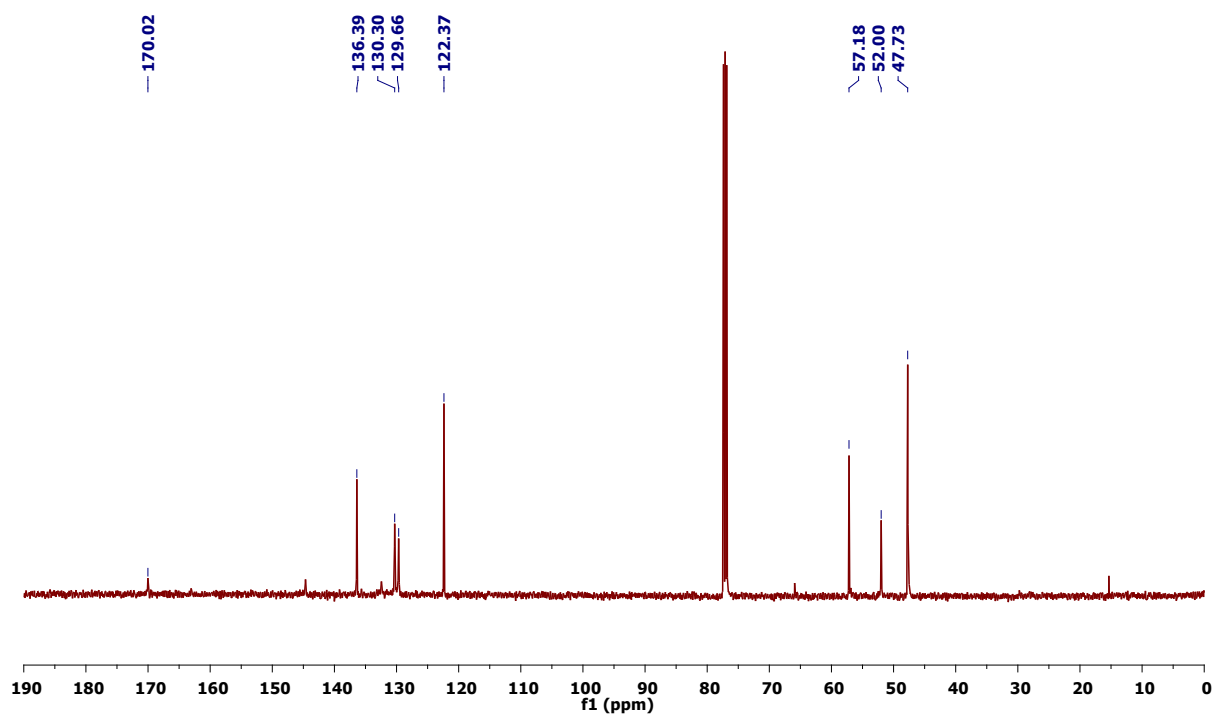
Figure S2 - ^{13}C NMR spectrum of complex 1
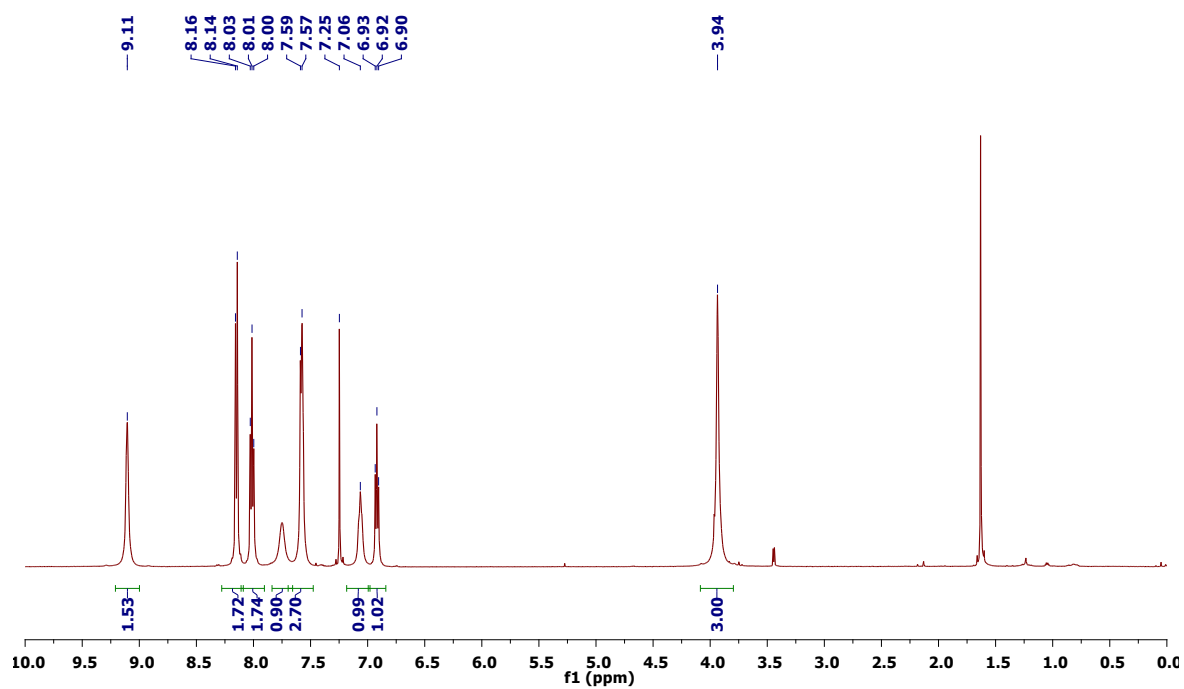
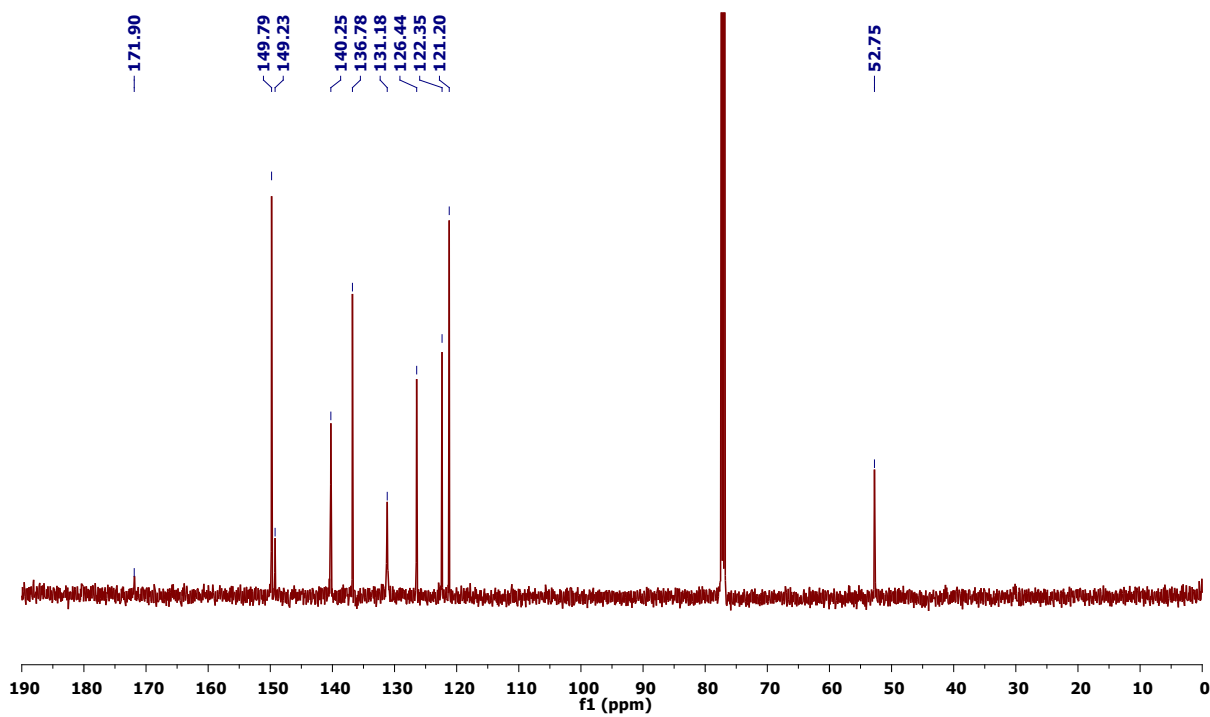FigureS3 - ^{1}H NMR spectrum of complex 2

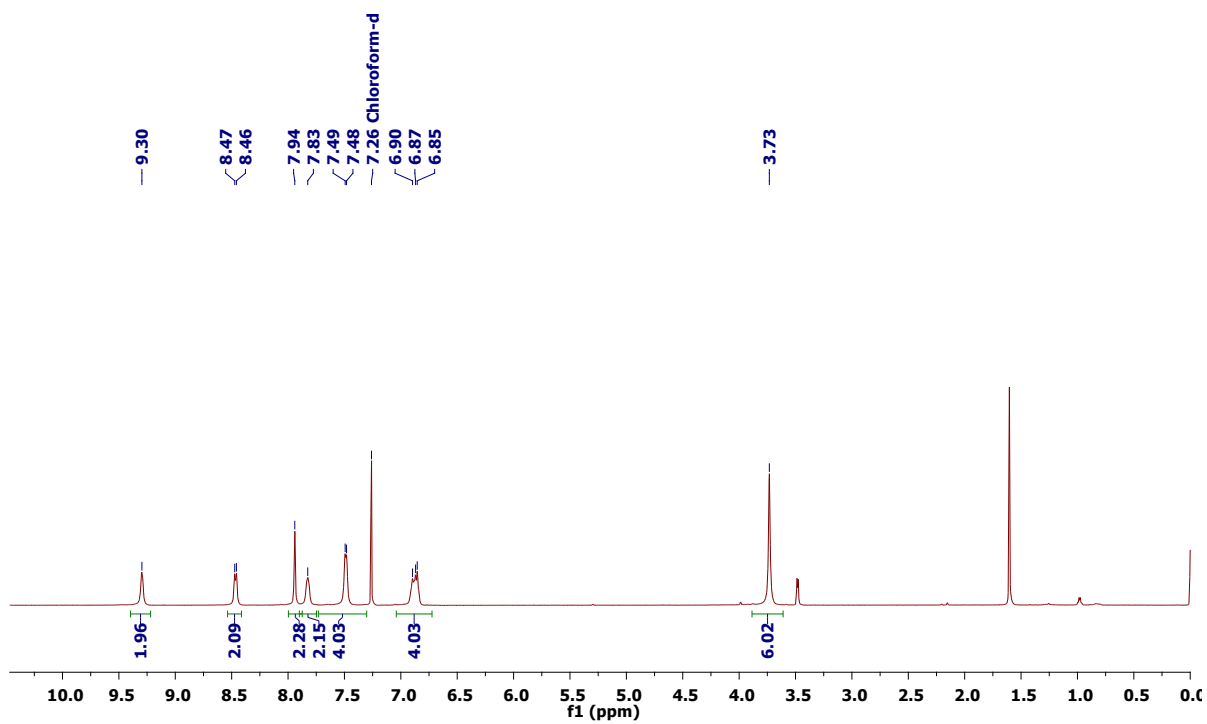Figure S4 - ^{13}C NMR spectrum of complex 2

Figure S5- ^{1}H NMR spectrum of complex 3
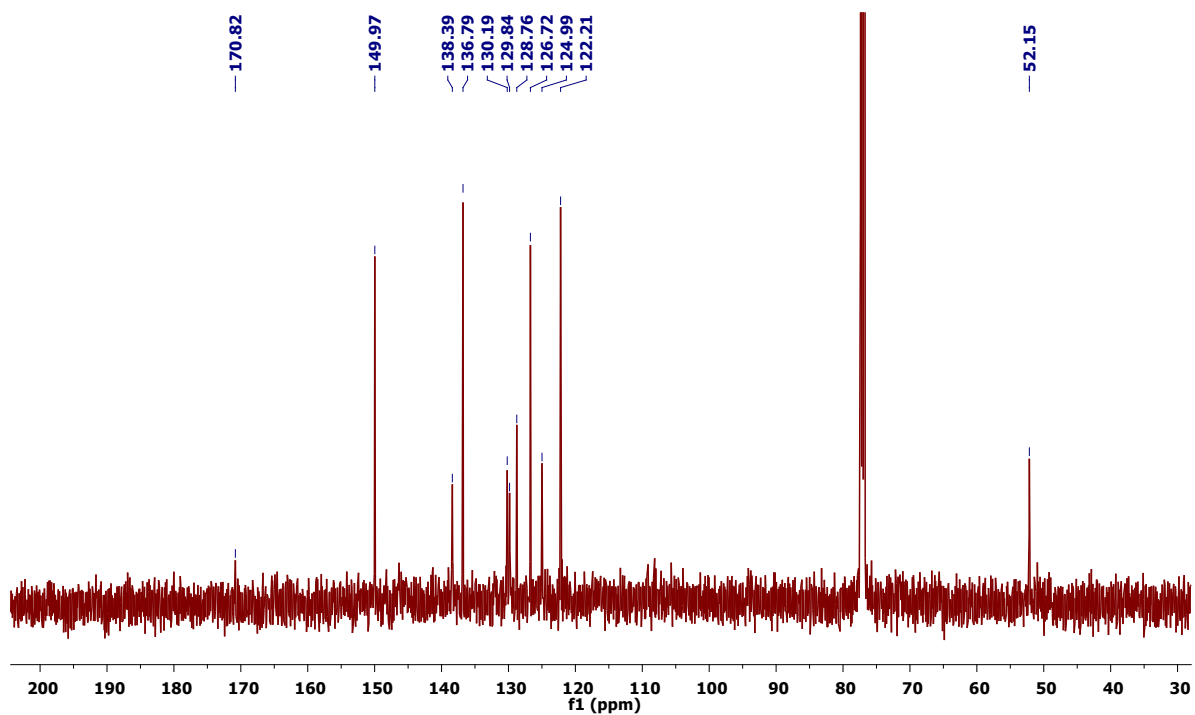
Figure S6- ^{13}C NMR spectrum of Complex 3

4
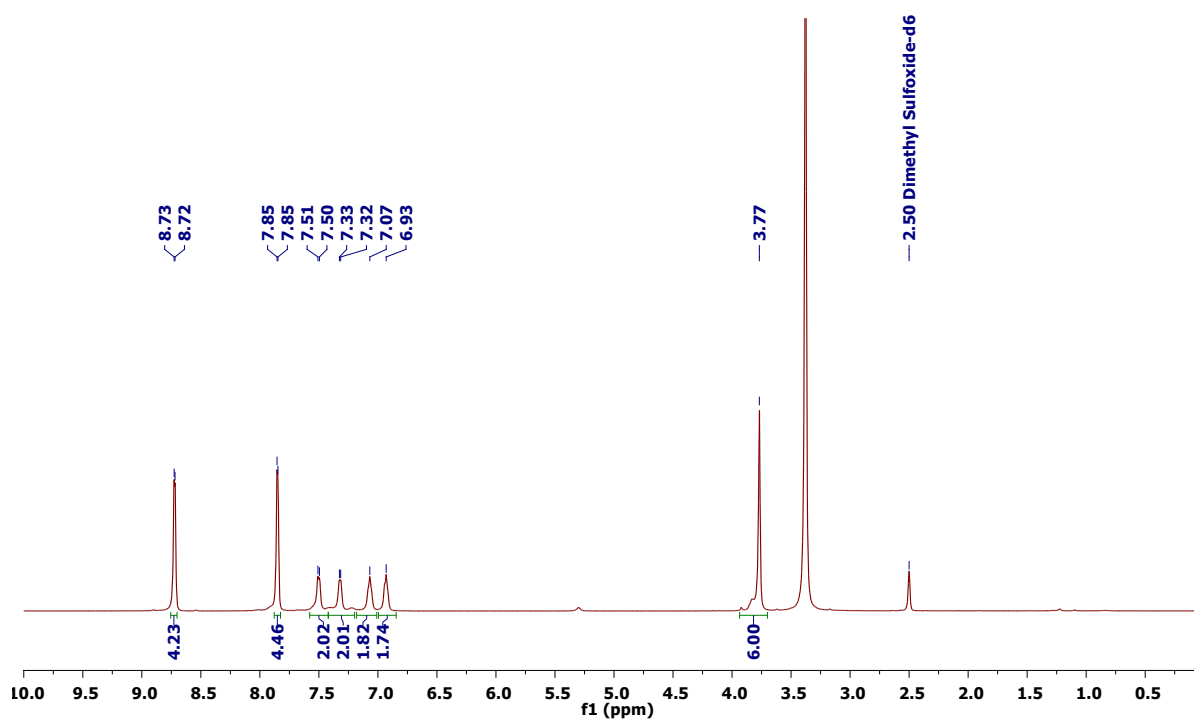
Figure S7 - ¹H NMR spectrum of Complex 4
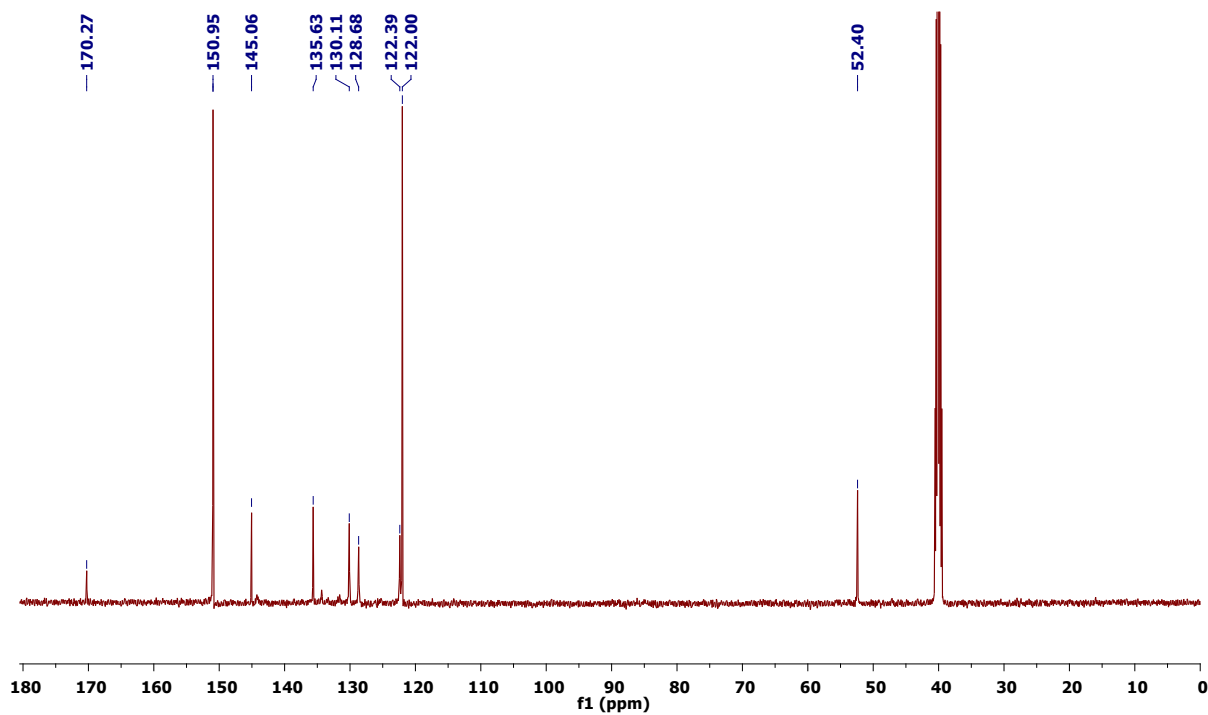
Figure S8- ¹³C NMR spectrum of Complex 4

Time dependent ^{1}H-NMR spectrum
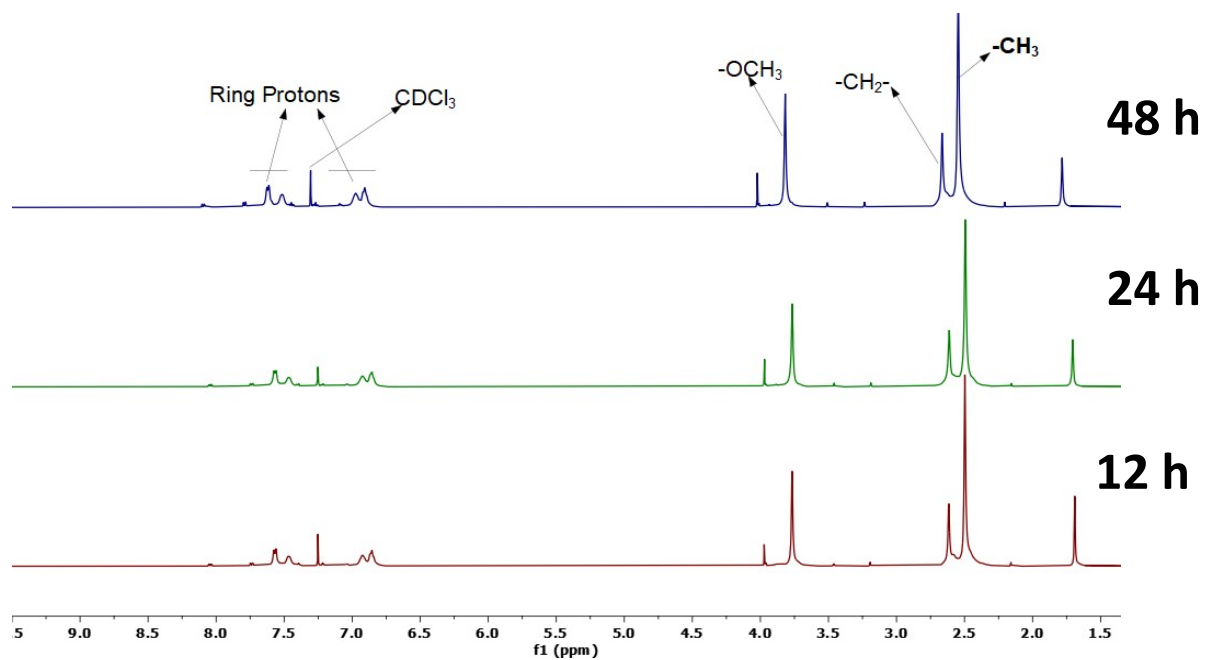
Figure 9 -Time dependent ^{1}H NMR spectra of Complex 1
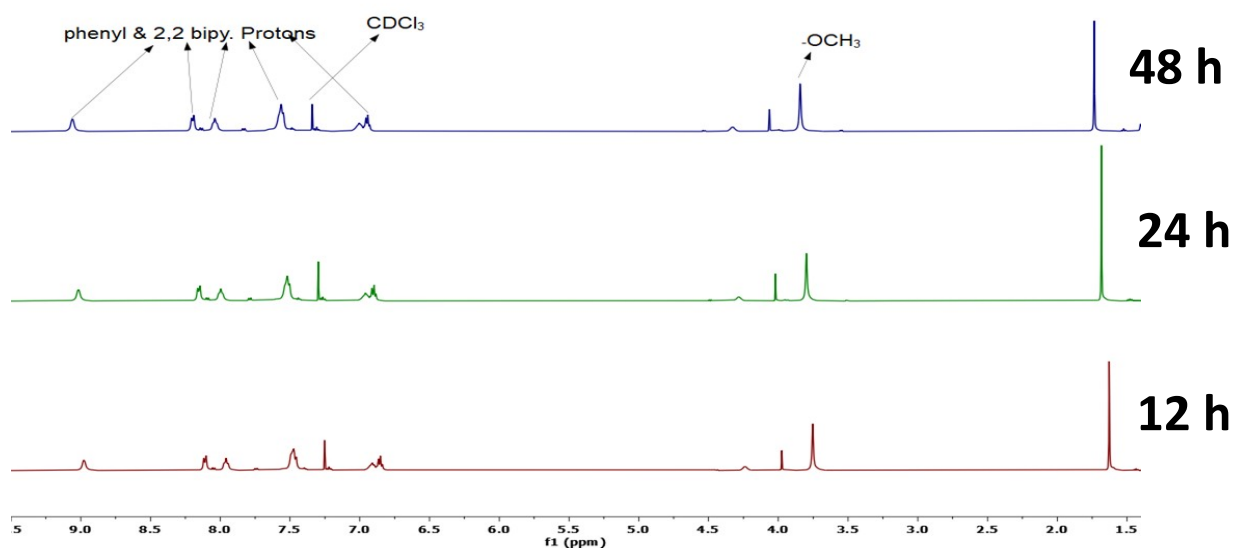
Figure10- Time dependent ^{1}H NMR spectra of Complex 2
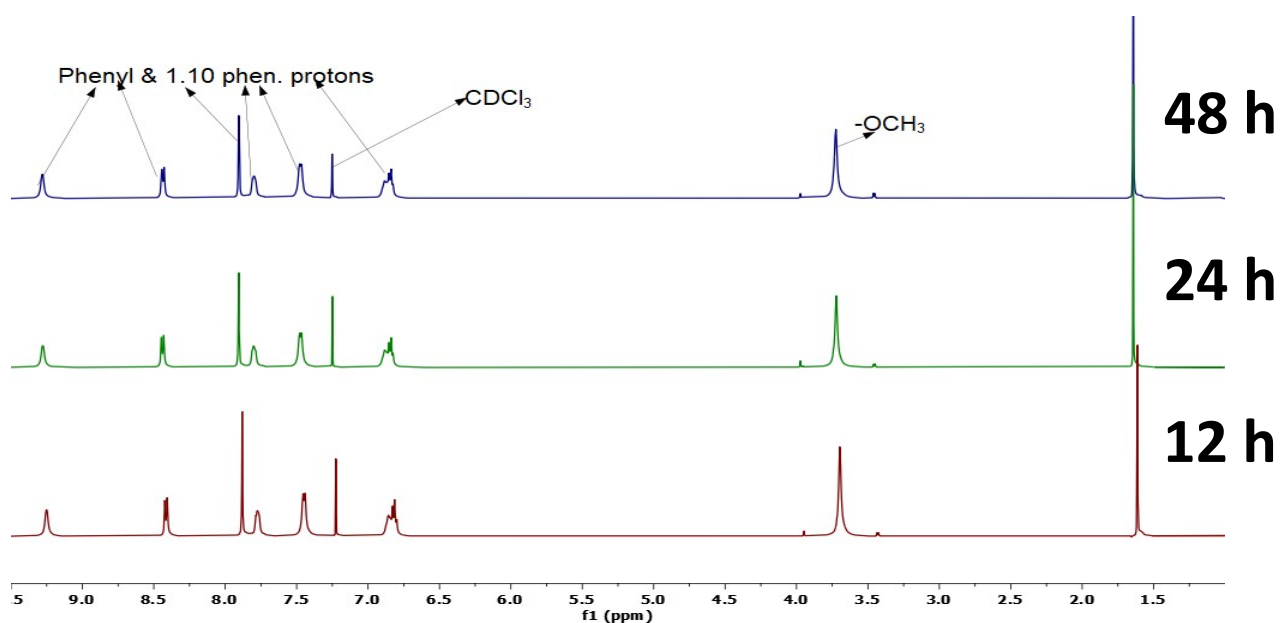
Figure 11 Time dependent ^{1}H NMR spectra of Complex 3
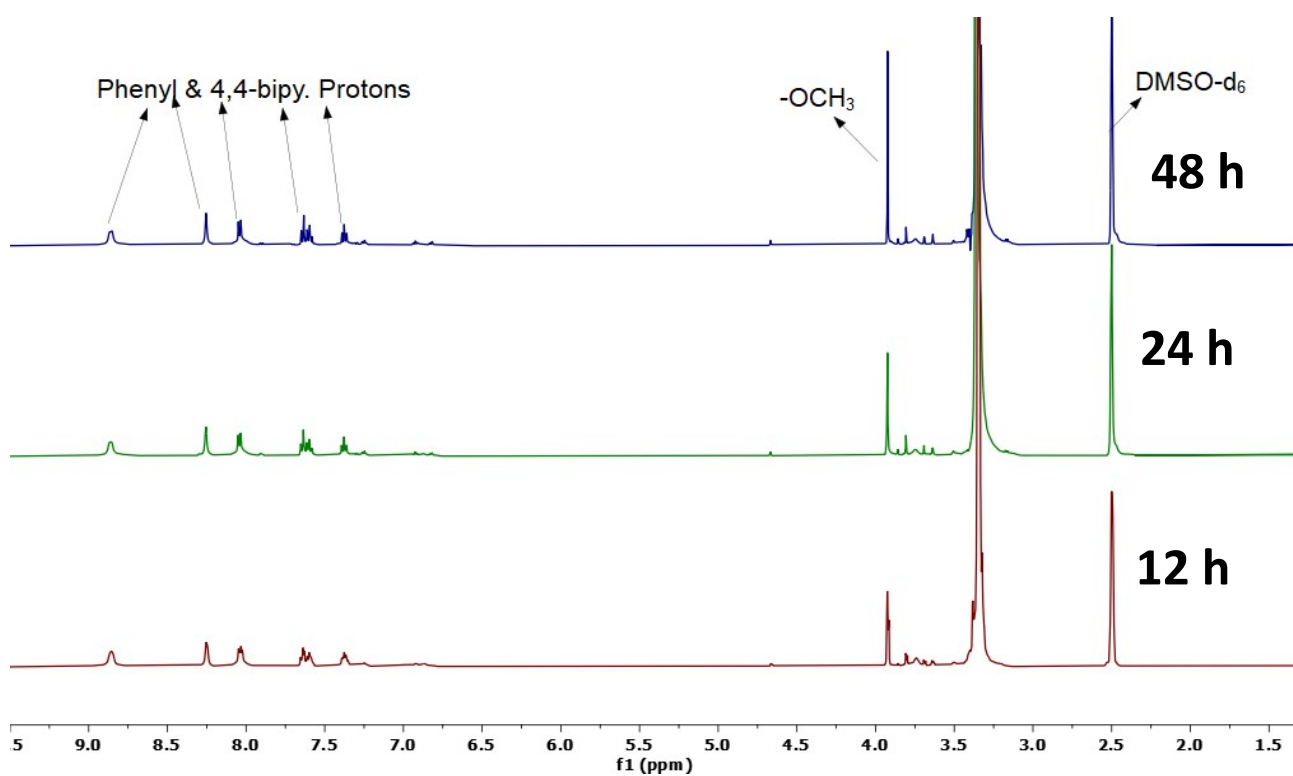
Figure 12 Time dependent ^{1}H NMR spectra of Complex 4
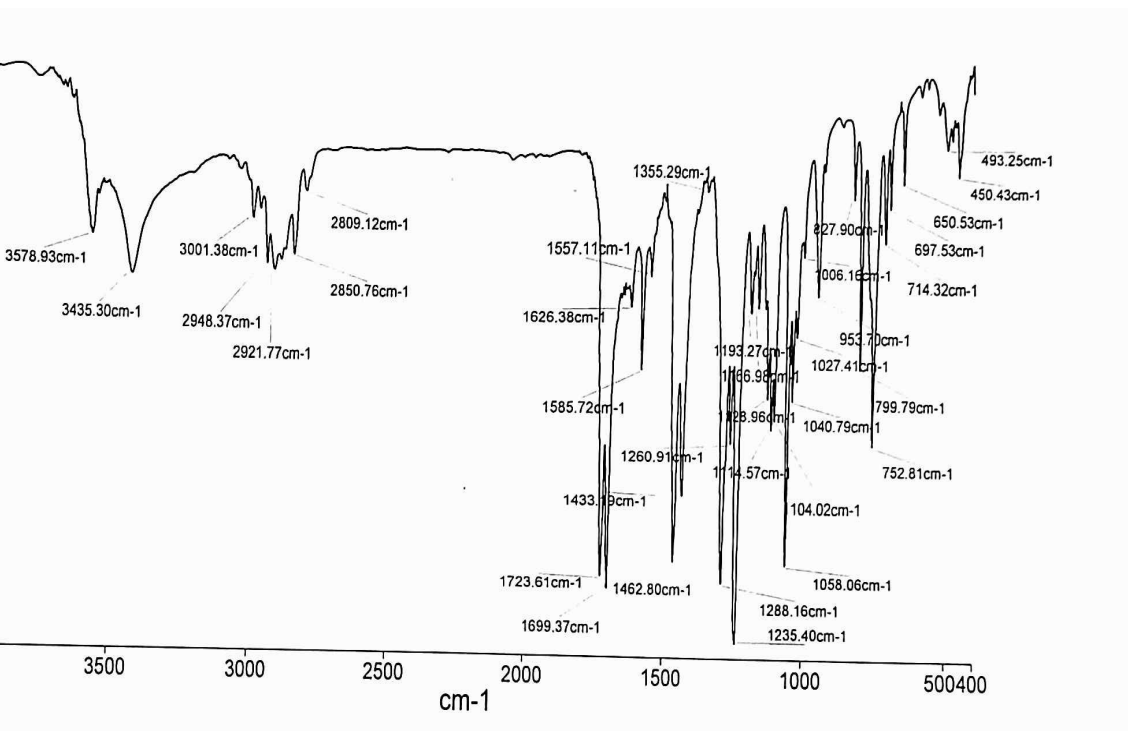
Figure S13. IR spectrum of Complex 1
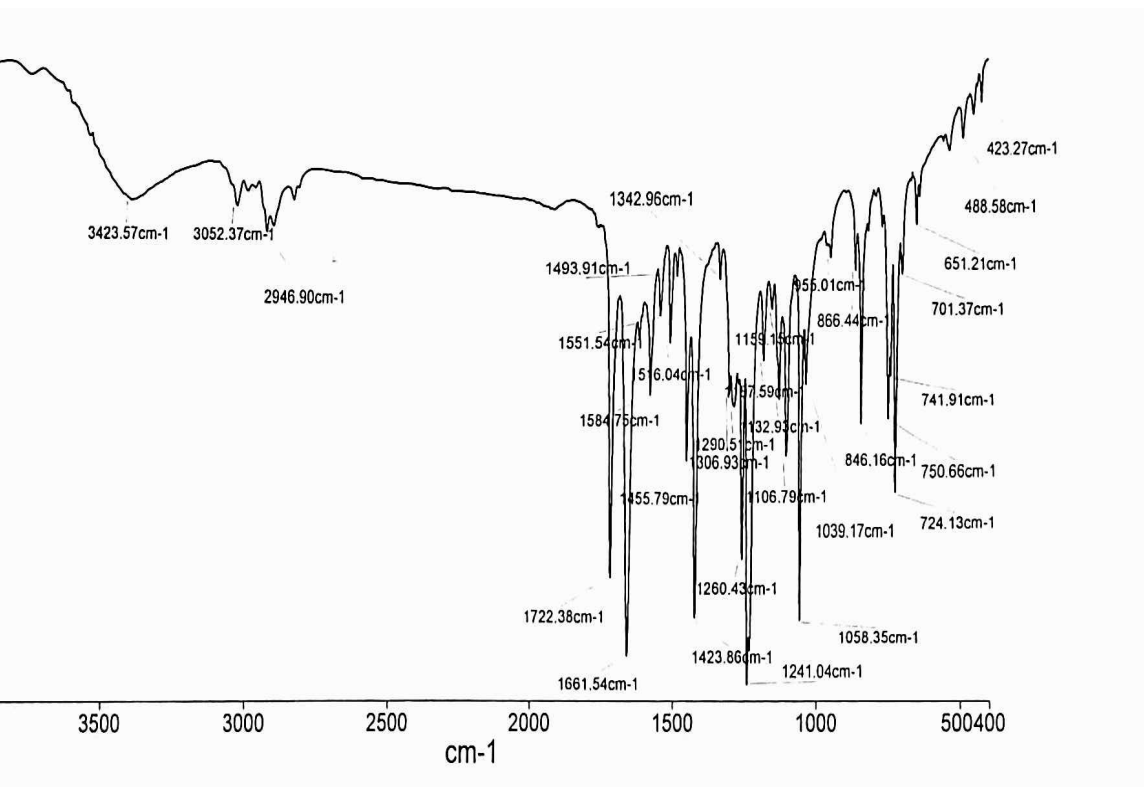
Figure S14. IR spectrum of Complex 2
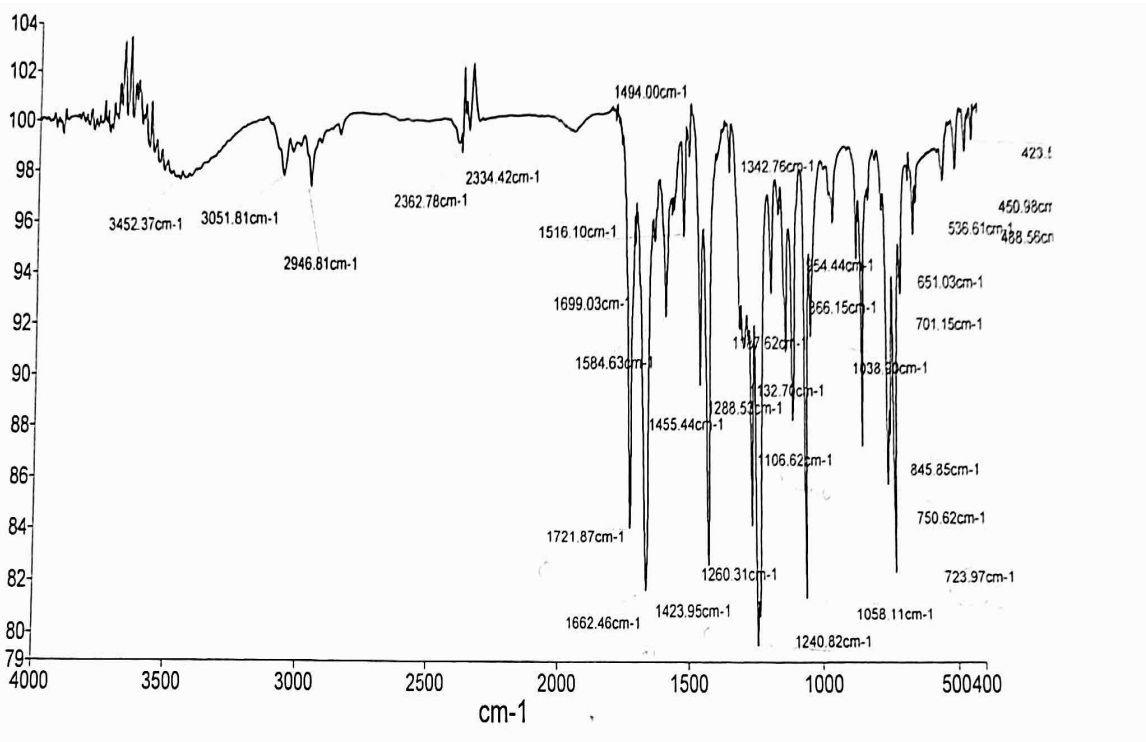
Figure S15. IR spectrum of Complex 3
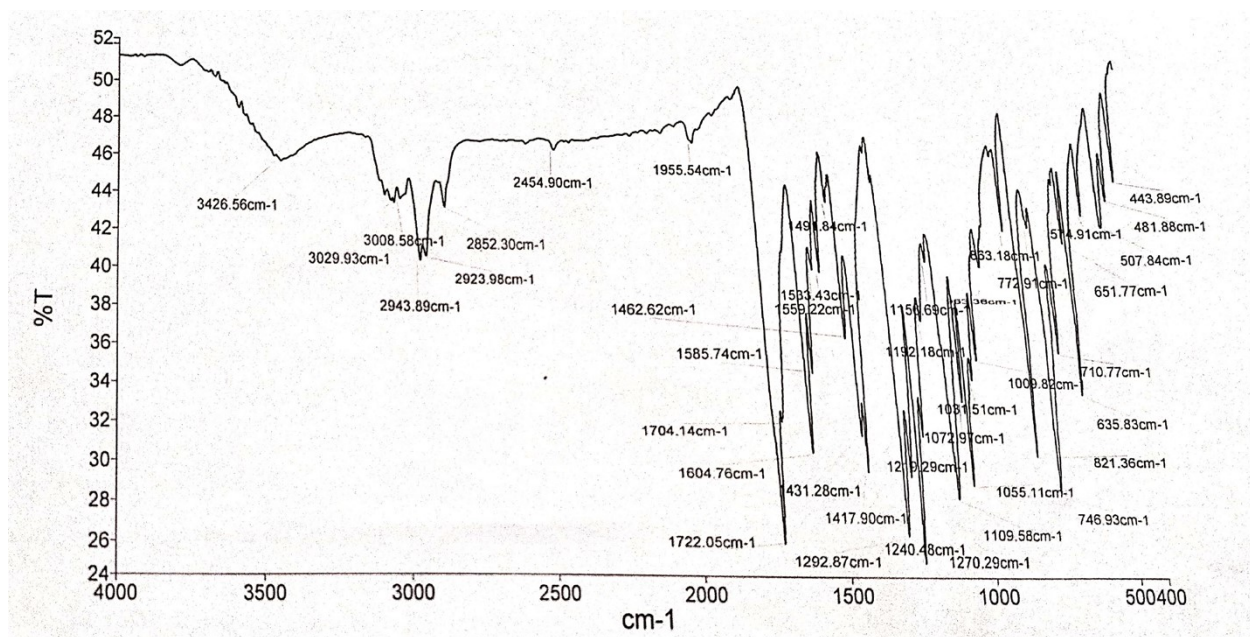
Figure S16. IR spectra of Complex-4

The conformation to existence of complexes 1-4 in both solid and liquid
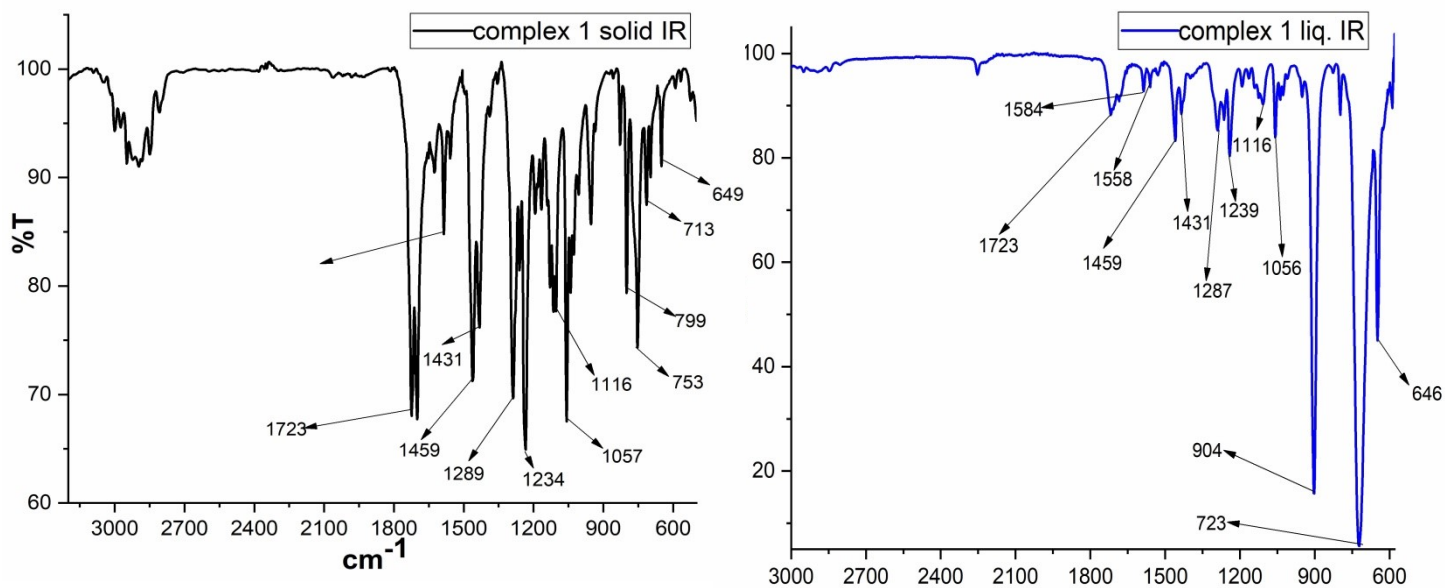
Figure S17 Solid and solution phase IR Spectra of complex 1

phase via Solid and Liquid IR spectrum
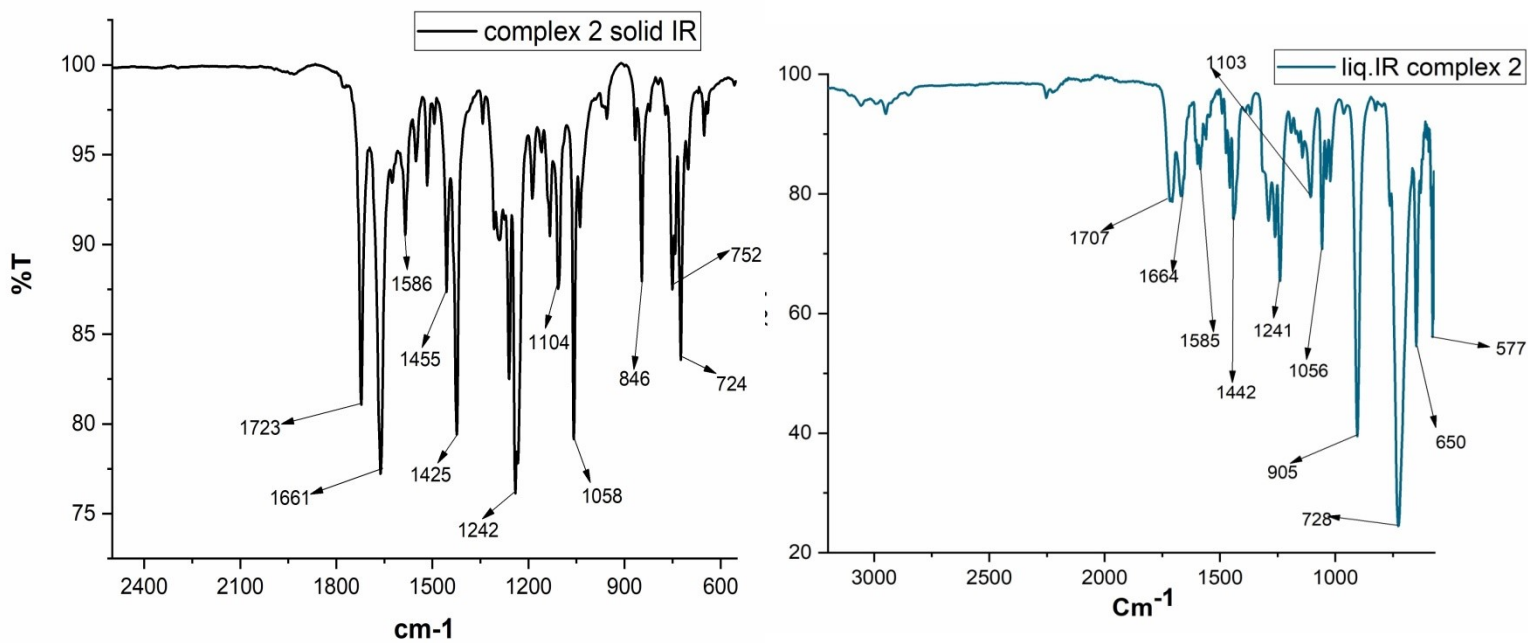
Figure S18 Solid and solution phase IR Spectra of complex 2
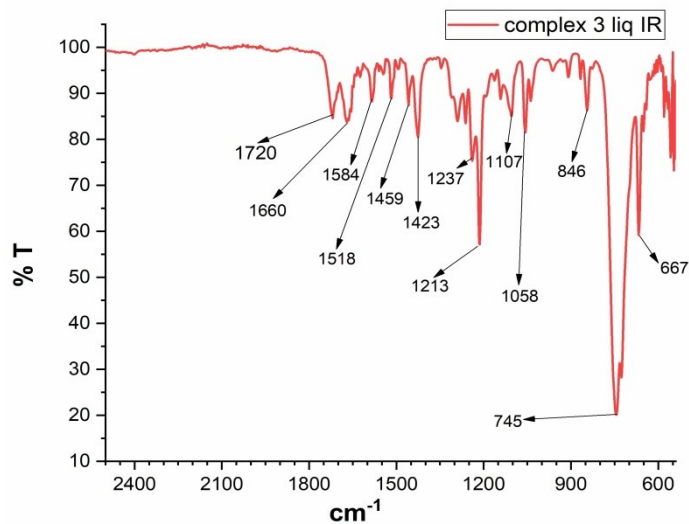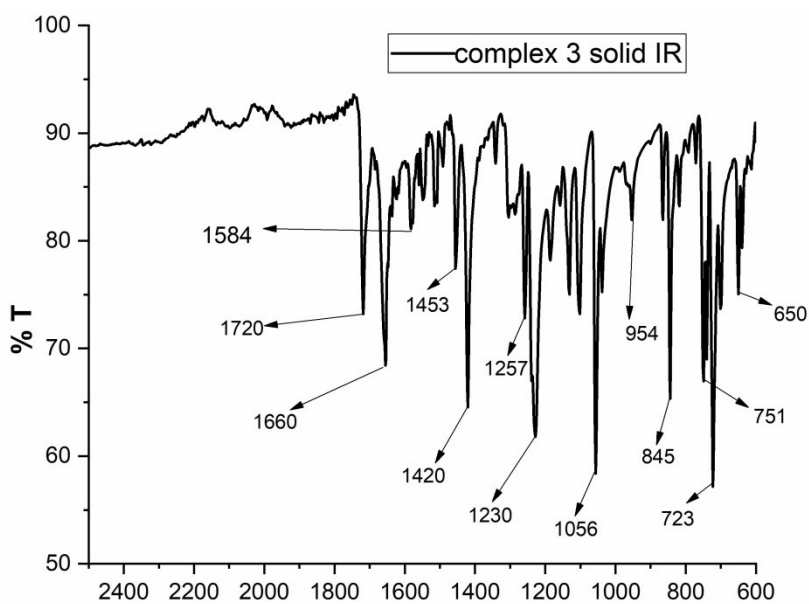
Figure S19 Solid and solution phase IR Spectra of complex 3
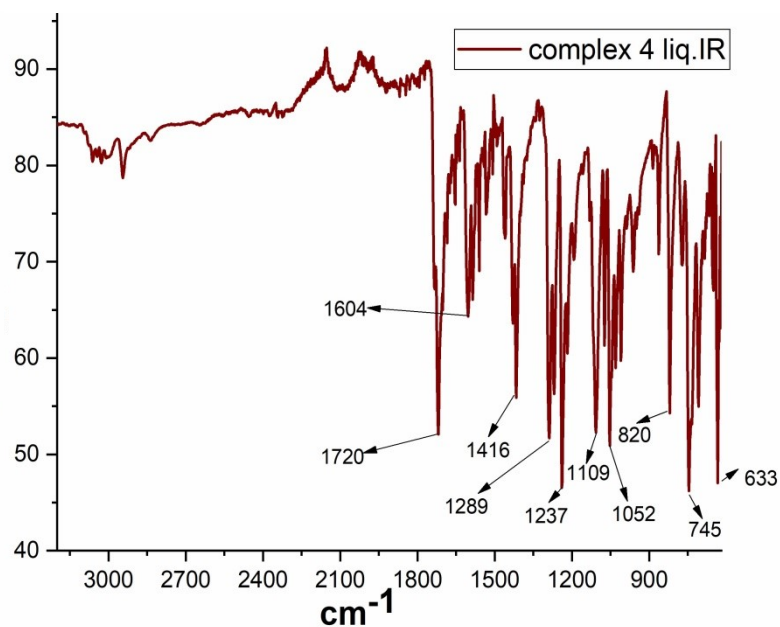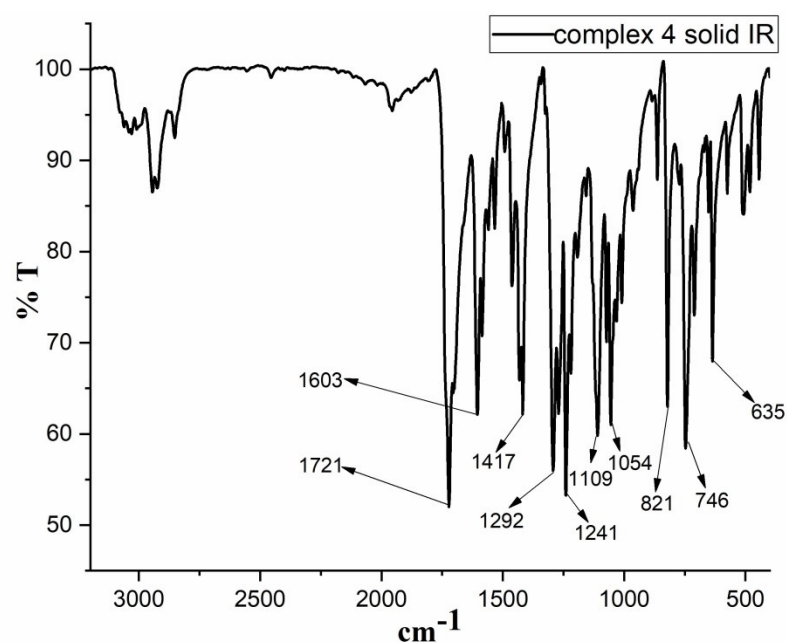
Figure S20 Solid and solution phase IR Spectra of complex 4
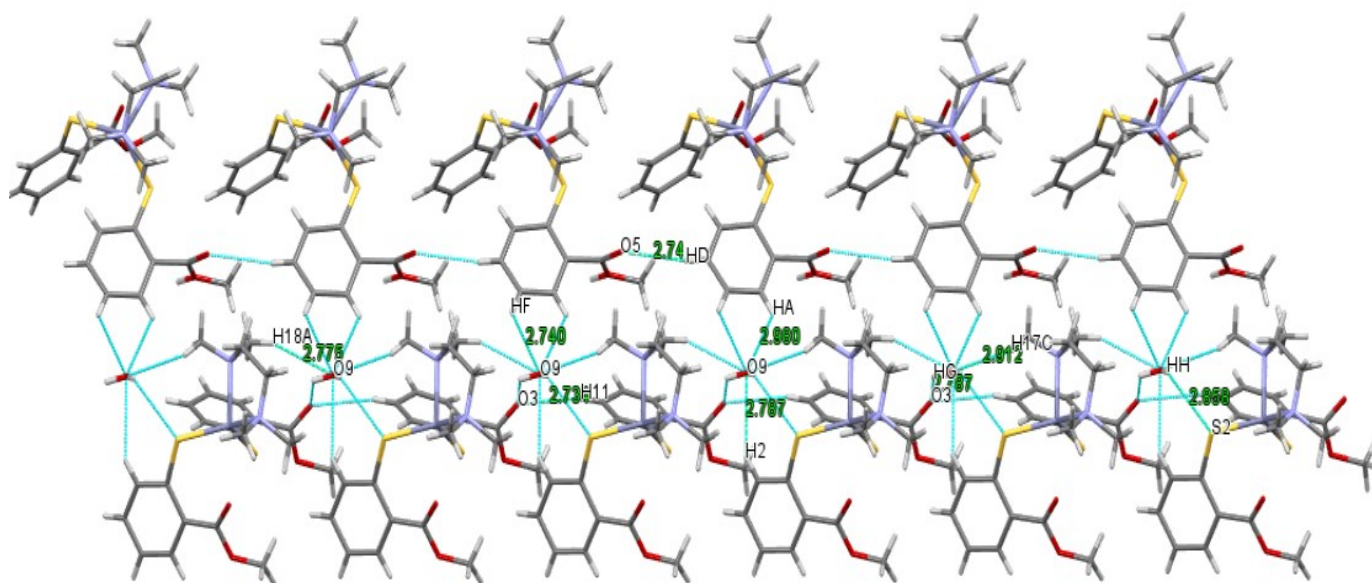
Figure S21. Packing diagram of **1** showing (sp^3)C-H···O(H$_2$O) , (sp^2)C-H···O(H$_2$O), (sp^2)C-H···O(C=O) and (H$_2$O)H···S interactions (blue dotted line).
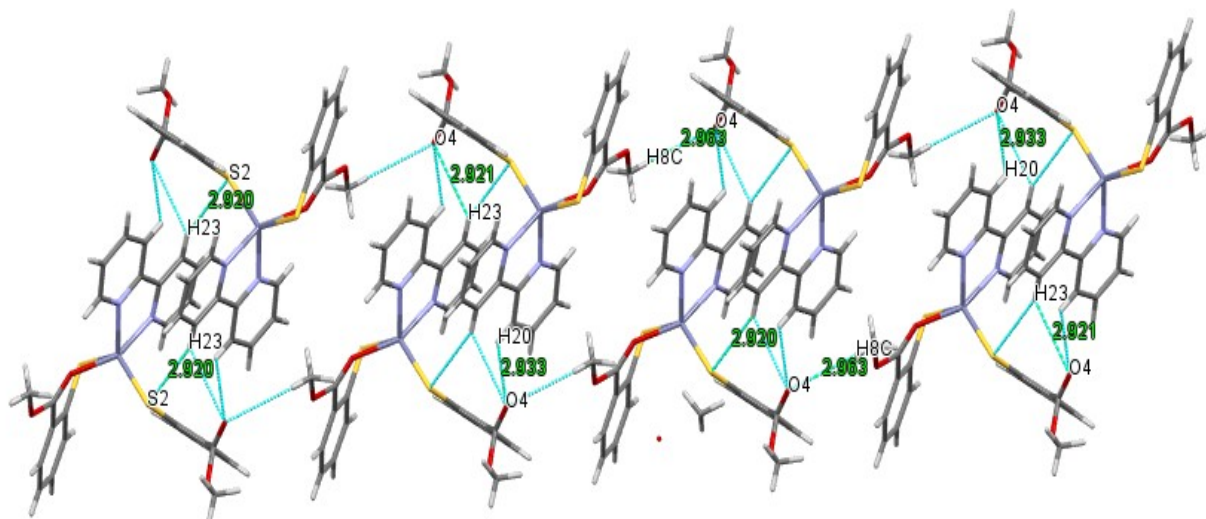
Figure S22. Packing diagram of **3** showing (sp^3)C-H···O, (sp^2)C-H···O, and (sp^2)C-H···S interactions (blue dotted line)
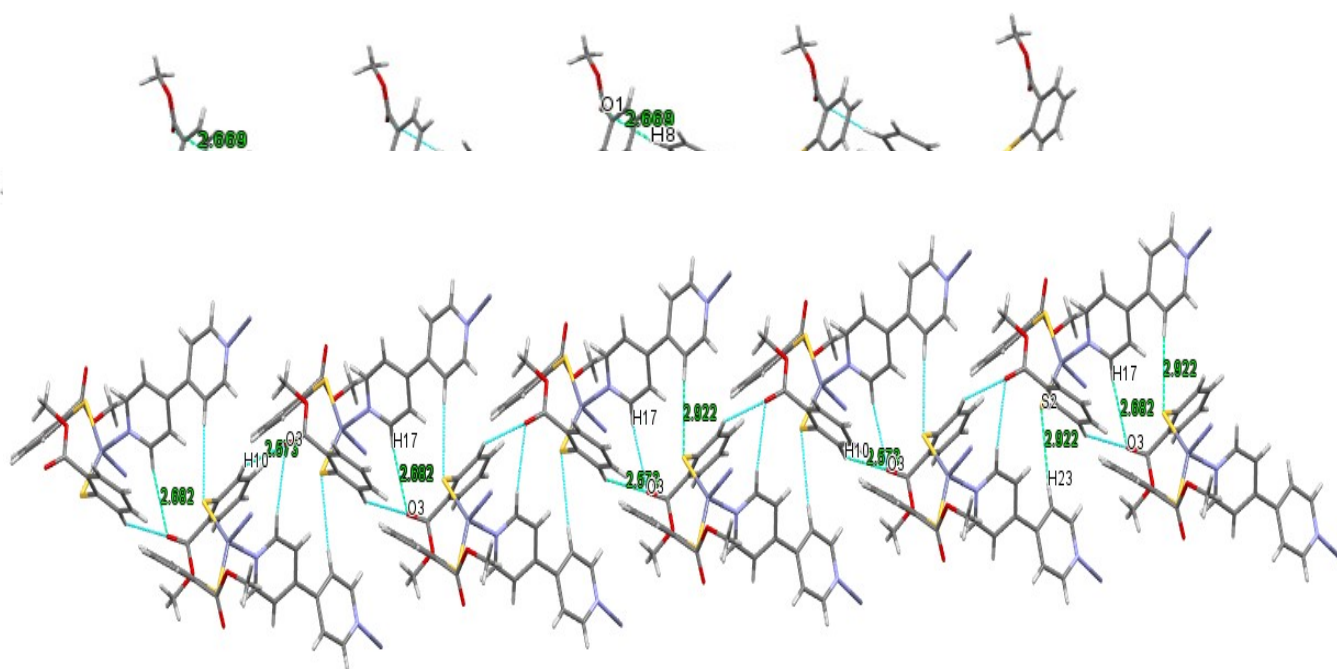
Figure S23. Packing diagram of **3** showing (sp^3) C-H$\cdots$O, (sp^2) C-H$\cdots$O, and (sp^2) C-H$\cdots$S interactions (green dotted line).

Figure 24 Packing diagram of **4** showing (sp^3) C-H$\cdots$O, (sp^2)C-H$\cdots$O, and (sp^2)C-H$\cdots$S interactions.

Calculated (DFT) and Experimental (Single Crystal X-ray Diffraction) Bond Lengths and Bond Angles

Table S1. For complex 1

Bond distance (Å)	Experimental (X-ray)	Calculated (DFT)
Zn(1)-S(2)	2.289(3)	2.318
Zn(1)-S(1)	2.287(3)	2.316
Zn(1)-N(1)	2.103(9)	2.205
Zn(1)-N(2)	2.173(9)	2.242

Bond Angle (Angle/°)	Experimental (X-ray)	Calculated (DFT)
S(1)-Zn(1)-S(2)	123.14(11)	127.50
N(1)-Zn(1)-S(2)	115.0(3)	120.17
N(1)-Zn(1)-S(1)	112.4(3)	100.06
N(1)-Zn(1)-N(2)	84.4(4)	84.40
N(2)-Zn(1)-S(2)	103.3(3)	106.49
N(2)-Zn(1)-S(1)	110.9(3)	109.86

Table S2- For complex 2

Bond distance (Å)	Experimental (X-ray)	Calculated (DFT)
Zn(1)-S(2)	2.3140(15)	2.333
Zn(1)-S(1)	2.278(14)	2.322

	Experimental (X-ray)	Calculated (DFT)
Zn(1)-O(1)	2.389(3)	2.322
Zn(1)-N(1)	2.115(4)	2.179
Zn(1)-N(2)	2.137(4)	2.222

Bond Angle (Angle/°)	Experimental (X-ray)	Calculated (DFT)
S(2)-Zn(1)-O(1)	87.01(10)	88.85
S(1)-Zn(1)-S(2)	124.30(5)	132.56
S(1)-Zn(1)-O(1)	82.48(9)	84.14
N(1)-Zn(1)-S(2)	110.43(10)	108.75
N(1)-Zn(1)-S(1)	122.89(10)	117.75
N(1)-Zn(1)-O(1)	85.50(13)	87.98
N(1)-Zn(1)-N(2)	76.62(15)	74.61
N(2)-Zn(1)-S(2)	109.46(11)	105.70
N(2)-Zn(1)-S(1)	97.86(11)	95.27
N(2)-Zn(1)-O(1)	158.95(14)	160.07

Table S3- For complex 3

Bond distance (Å)	Experimental (X-ray)	Calculated (DFT)
Zn(1)-S(2)	2.299(3)	2.322
Zn(1)-S(1)	2.280(3)	2.319
Zn(1)-O(1)	2.302(6)	2.331
Zn(1)-N(2)	2.142(7)	2.180
Zn(1)-N(1)	2.193(8)	2.283

Bond Angle (Angle/°)	Experimental (X-ray)	Calculated (DFT)
S(2)-Zn(1)-O(1)	102.54(2)	92.48
S(1)-Zn(1)-S(2)	131.04(12)	138.48
S(1)-Zn(1)-O(1)	84.2(2)	84.99
N(2)-Zn(1)-S(2)	95.2(2)	101.38
N(2)-Zn(1)-S(1)	133.7(2)	114.07
N(2)-Zn(1)-O(1)	85.1(3)	85.06
N(2)-Zn(1)-N(1)	76.73(3)	74.96
N(1)-Zn(1)-S(2)	104.89(2)	106.67
N(1)-Zn(1)-S(1)	89.73(2)	94.51
N(1)-Zn(1)-O(1)	148.3(3)	158.98

Table S4-For complex 4

Bond distance (Å)	Experimental (X-ray)	Calculated (DFT)
Zn(1)-S(1)	2.280(5)	2.260
Zn(1)-S(2)	2.274(5)	2.260
Zn(1)-N(2)	2.095(15)	1.946
Zn(1)-N(1)[1]	2.112(15)	1.958

Bond Angle (Angle/°)	Experimental (X-ray)	Calculated (DFT)
S(2)-Zn(1)-S(1)	126.78(2)	113.36
N(2)-Z(1)-S(1)	104.17(5)	104.59
N(2)-Zn(1)-S(2)	111.54(5)	112.16
N(2)-Zn(1)-N(1)1	93.48(6)	107.20
N(1)1-Zn(1)-S(1)	107.38(5)	107.67
N(1)1-Zn(1)-S(2)	108.38(4)	111.72

Table S5 - Second Order Perturbation Theory Analysis of complex 2

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j)-E(i) a.u.	F(i,j) a.u.
LP (1) O 4	LP*(6)Zn 1	6.51	0.74	0.068
LP (1) O 4	LP*(9)Zn 1	21.34	0.82	0.119
LP (3) S 3	LP*(6)Zn 1	67.92	0.35	0.142
LP (3) S 3	LP*(7)Zn 1	34.41	0.45	0.114
LP (3) S 3	LP*(8)Zn 1	1.70	0.39	0.024
LP (3) S 3	LP*(9)Zn 1	1.47	0.43	0.024
LP (3) S 2	LP*(6)Zn 1	89.34	0.34	0.161
LP (3) S 2	LP*(7)Zn 1	40.82	0.45	0.124
LP (3) S 2	LP*(8)Zn 1	3.63	0.39	0.035
LP (1) S 2	LP*(9)Zn 1	1.91	0.54	0.029
LP (1) N 5	LP*(6)Zn 1	14.35	0.47	0.080
LP (1) N 5	LP*(8)Zn 1	31.61	0.52	0.115
LP (1) N 7	LP*(6)Zn 1	15.77	0.47	0.083
LP (1) N 7	LP*(8)Zn 1	8.74	0.51	0.060
LP (1) N 7	LP*(9)Zn 1	21.72	0.55	0.098

Table S6- Second Order Perturbation Theory Analysis of complex 3

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j)-E(i) a.u.	F(i,j) a.u.
LP (1) N 6	LP*(6)Zn 1	12.86	0.47	0.076
LP (1) N 6	LP*(8)Zn 1	27.69	0.53	0.109
LP (1) N 6	LP*(9)Zn 1	7.05	0.55	0.056
LP (1) N 7	LP*(6)Zn 1	13.25	0.46	0.076
LP (1) N 7	LP*(8)Zn 1	15.97	0.52	0.082
LP (1) N 7	LP*(9)Zn 1	12.88	0.54	0.075
LP (3) S 2	LP*(6)Zn 1	87.75	0.35	0.162
LP (3) S 2	LP*(7)Zn 1	49.22	0.47	0.139
LP (2) S 2	LP*(8)Zn 1	9.62	0.34	0.051
LP (2) S 2	LP*(9)Zn 1	2.11	0.36	0.025
LP (3) S 3	LP*(6)Zn 1	69.96	0.36	0.148
LP (3) S 3	LP*(7)Zn 1	40.16	0.48	0.126
LP (3) S 3	LP*(8)Zn 1	1.75	0.42	0.025
LP (1) O 4	LP*(6)Zn 1	6.48	0.74	0.069
LP (1) O 4	LP*(9)Zn 1	21.44	0.81	0.120

UV–Vis absorption spectra (Experimental and Calculated)

Figure –S25-(a)U V spectrum of complex 1 (b) Selected molecular orbitals of complex 1 showing electronic transitions (orbital contour value = 0.02).
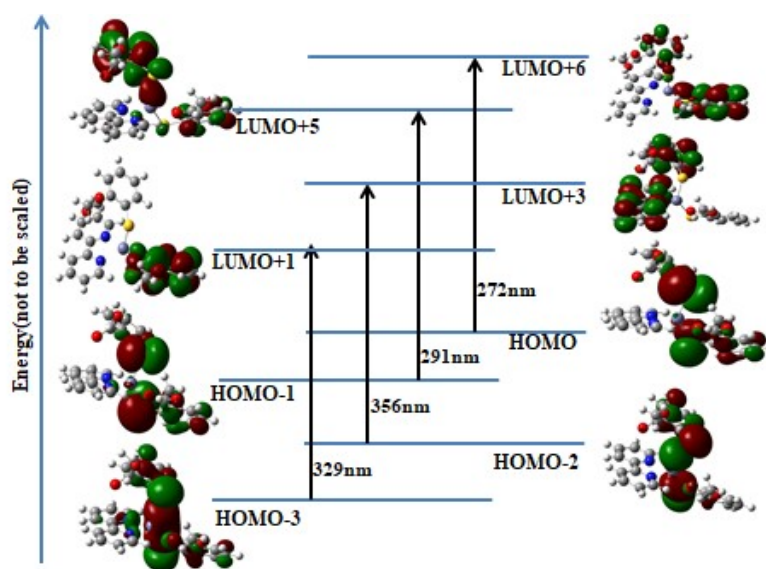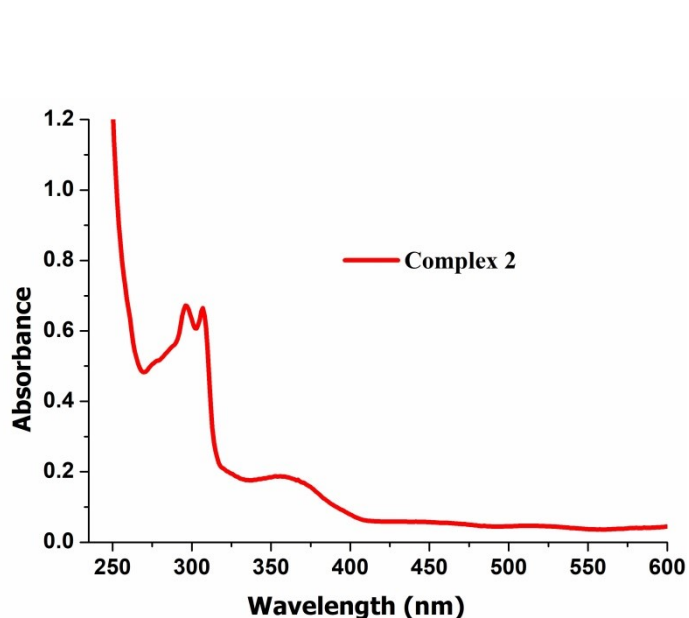
Fugure S26-(a) U V spectrum of complex 2 (b) Selected molecular orbitals of complex 2 showing electronic transitions (orbital contour value = 0.02).
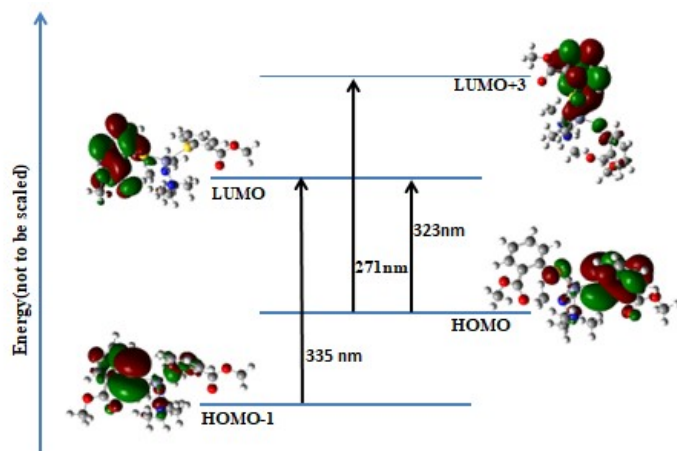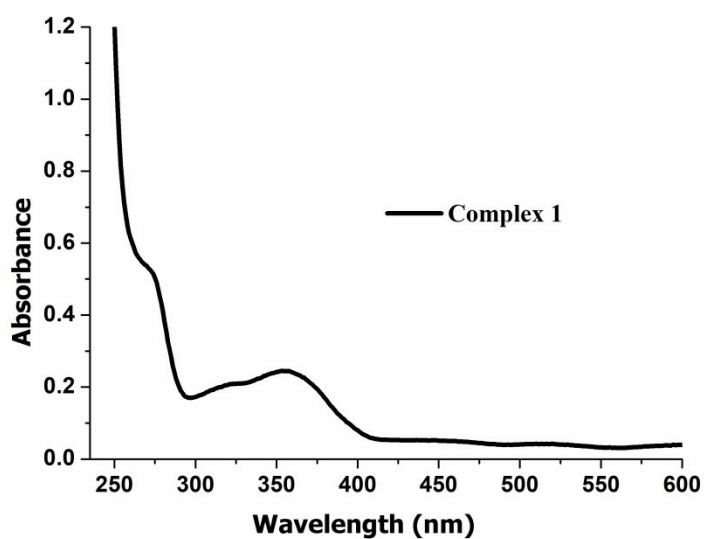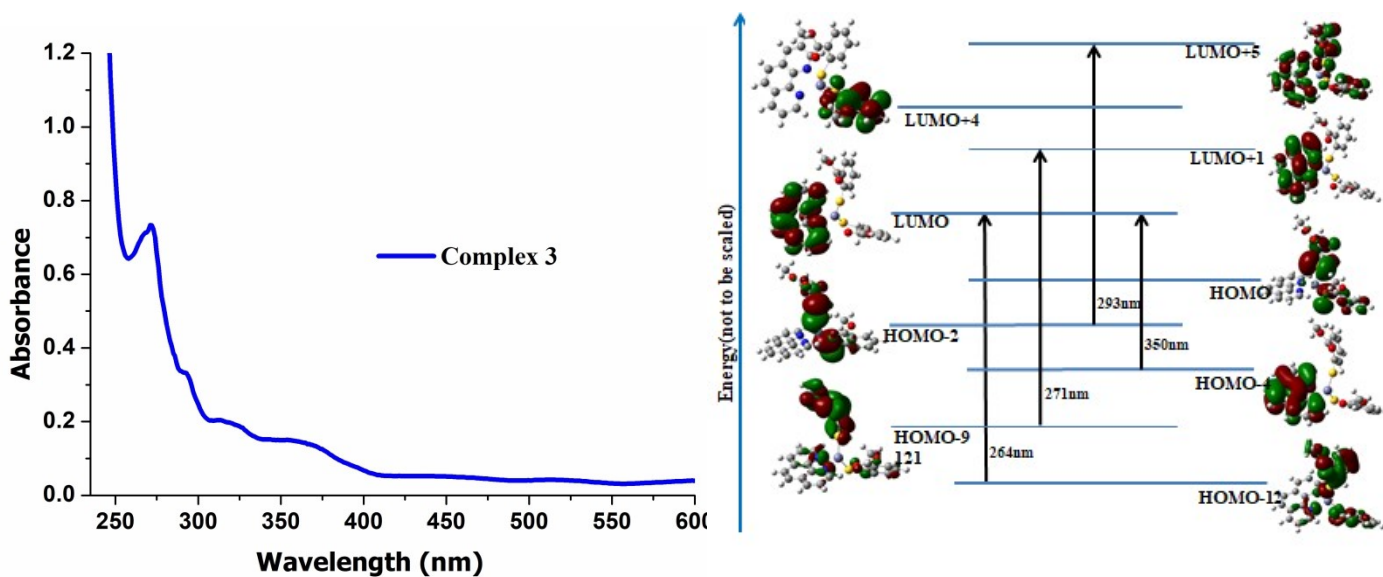
Figure –S27 (a) U V spectrum of complex 3 (b) Selected molecular orbitals of complex 3 showing electronic transitions (orbital contour value = 0.02).
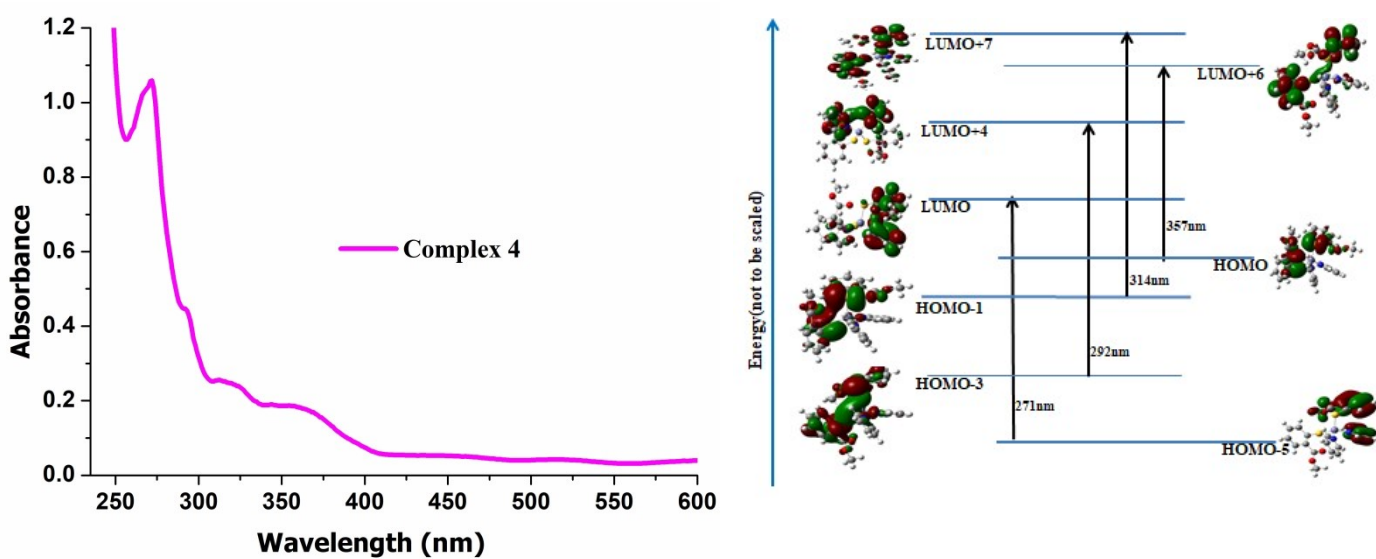
Figure –S28 (a) U V spectrum of complex 4 **(b)** Rrepresented Selected molecular orbitals of complex 4 showing electronic transitions (orbital contour value = 0.02).

Molecular docking results of Complex 1-4 with the targeted proteins expressed in cancer

				Table S7. For complex 1			
Proteins	**Pocket ID**	**Vina Score**	**Cavity volume (Å3)**	**Interacting amino acids**			
VEGF	C1	-5.2	95	**Chain E**: TYR139 SER140 GLU141 PHE172 PRO173 LEU204 THR206 GLU208 LYS217 THR218 ASN219			
	C2	-4.9	84	**Chain E**: PRO163 ASN164 ILE165 THR166 VAL167 PRO179 GLY181 ILE184 ILE185 TRP186 ASP187 PHE192			
	C3	-4.8	83	**Chain E**: ARG133 PRO134 THR161 SER162 ASN164 ILE165 THR166 THR210 VAL211 ASN212			
	C4	-4.6	77	**Chain E**: THR166 VAL167 THR168 LEU169 LYS170 THR176 LEU177 ILE178 PRO179 GLU208 ALA209 THR210 LEU215			
	C5	-5.5	73	**Chain E**: GLU144 ILE145 ILE146 HIS147 MET148 THR149 ARG152 GLU153 LEU154 VAL155 PRO157 GLN225			
TGFB1	C1	-5.1	126	**Chain A**: LEU20 ILE22 LEU28 TRP30 TYR39 ALA41 ASN42 PHE43 CYS44 CYS78 PRO80 LEU83 ASN103 MET104 VAL106			
	C2	-4.9	83	**Chain A**: CYS7 PHE8 SER10 THR11 GLU12 LYS13 CYS16 VAL17 ARG18 GLN19 PHE43 LEU45 GLY46			
	C3	-5.3	56	**Chain A**: PRO47 CYS48 PRO49 TYR50 ALA63 ASN66 GLN67 PRO70 GLY71 ALA72 ALA75 PRO76			
	C4	-5.1	49	**Chain A**: THR4 PHE8 GLN19 PRO36 TYR39 HIS40 ASN42 GLU84 LEU86 PRO87 ILE105 VAL106 ARG107			
	C5	-5	44	**Chain A**: CYS7 PHE8 SER10 THR11 GLU12 LYS13 CYS16 VAL17 ARG18 GLN19 PHE43 LEU45 GLY46			
BRAF	C1	-6.8	2436	**Chain A**: ILE463 GLY464 VAL471 ALA481 LYS483 GLN530 TRP531 CYS532 GLY534 SER535 SER536 HIS539 ASN580 PHE583 ASP594 PHE595 LEU597			
	C2			**Chain B**: SER467 ALA497 ASN500 GLU501 VAL504 LEU505 THR508 LEU567 ILE572			

				ILE573 HIS574 ARG575 ASP576 GLY593 ASP594
	C3	-6.6	1855	**Chain A**: VAL511 ASP555 ARG558 GLN559 ARG562 ASN588 THR589
				Chain B: ASP479 GLN530 TRP531 GLU533 HIS585 GLU586
	C4	-7.2	1065	**Chain A**: ALA497 ASN500 GLU501 VAL504 LEU505 LEU567 ILE572 ILE573 HIS574 ARG575 ASP576 GLY593 ASP594 GLY596 THR599
	C5	-4.1	309	**Chain B**: LEU674 SER675 PRO676 ASP677 LEU678 MET693 ALA694 LEU697 LYS698 LYS699
p53	C1	-5.7	413	**Chain B**: SER1742 ASP1743 ALA1746 HIS1809 ARG1811 TYR1852 LEU1854 GLU1945 GLN1949 LYS1964 TYR1969
	C2	-6.8	272	**Chain B**: LEU1931 ALA1934 GLU1935 GLN1938 LEU1939 PRO1940 VAL1941 VAL1942 PHE1959 LYS1960 HIS1962 TYR1965 LYS1966 HIS1967 ASP1968
	C3	-4.7	265	**Chain B**: PRO1769 PRO1770 PHE1771 ASP1807 SER1827 HIS1828 VAL1829 HIS1832 ASP1833
	C4	-5.1	187	**Chain B**: GLN1801 GLY1822 PRO1824 TYR1843 ARG1844 LEU1847 TRP1862 PRO1864 ARG1865
	C5	-6	113	**Chain B**: ARG1811 PHE1884 THR1922 ASP1923 PRO1924 SER1943 GLN1944 GLU1945 LYS1964 HIS1967 TYR1969 VAL1970
BSA	C1	-6	8389	**Chain A**: THR190 ARG194 ARG217 GLN220 ALA290 GLU291 LYS294 GLU339 TYR340 ALA341 VAL342 LYS439 GLU443 PRO446 CYS447 ASP450 TYR451
	C2	-6.3	3498	**Chain A**: ASP108 SER109 PRO110 ASP111 LEU112 PRO113 LYS114 ARG144 PRO420 VAL423 GLU424 ARG458 ILE522
	C3	-5.2	1508	**Chain A**: GLU503 LYS504 PHE506 THR507 PHE508 HIS509 ALA568 GLY571 PRO572 VAL575
	C4	-5.6	793	**Chain A**: GLU100 LEU103 SER104 ILE202 GLN203 LYS204 LYS242 CYS245 HIS246 ASP248
	C5			**Chain A**: LEU386 GLN389 ASN390 GLN393

				VAL408 ARG409 ARG412 LYS413 SER488 LEU490 THR491 PRO492

Table S8. For complex 2				
Proteins	**Pocket ID**	**Vina Score**	**Cavity volume (Å3)**	**Interacting amino acids**
VEGF	C1	-6	95	**Chain E**: SER140 GLU141 LYS170 LYS171 PHE172 PRO173 LEU174 LEU204 THR206 GLU208 LYS217 ASN219
	C2	-5.3	84	**Chain E**: PRO163 ASN164 ILE165 THR166 VAL167 PRO179 ASP180 GLY181 ILE184 ILE185 TRP186 SER188
	C3	-4.8	83	**Chain E**: ARG133 PRO134 THR161 SER162 ASN164 ILE165 THR210 VAL211 ASN212
	C4	-4.7	77	**Chain E**: ARG133 PRO134 THR161 SER162 ASN164 ILE165 THR210 VAL211 ASN212
	C5	-5.7	73	**Chain E**: GLU137 GLU144 ILE145 ILE146 HIS147 GLU153 LEU154 VAL155 PRO157 ARG159 ARG189 LYS190
TGFB1	C1	-5.6	126	**Chain A**: LEU20 ILE22 LEU28 TYR39 ALA41 ASN42 PHE43 CYS44 CYS78 VAL79 PRO80 LEU83 ASN103 MET104 ILE105 VAL106
	C2	-5	83	**Chain A**: ASP23 PHE24 ARG25 TRP30 LYS31 TRP32 ILE33 HIS34 GLU35 PRO36 LYS37
	C3	-5.9	56	**Chain A**: PRO47 CYS48 PRO49 TYR50 ALA63 ASN66 GLN67 PRO70 GLY71 ALA72 ALA75 PRO76
	C4	-5.9	49	**Chain A**: THR4 PHE8 GLN19 TYR21 PRO36 GLY38 TYR39 HIS40 ASN42 GLU84 PRO85 LEU86 PRO87 ILE105 VAL106 ARG107
	C5	-5.9	44	**Chain A**: CYS7 SER10 THR11 GLU12 LYS13 CYS16 ARG18 GLN19 PHE43 LEU45
BRAF	C1	-8.2	2436	**Chain A**: ILE463 GLY464 SER465 VAL471 ALA481 LYS483 LEU514 TRP531 CYS532 GLY534 SER535 SER536 HIS539 ASN580 PHE583 ASP594 PHE595 LEU597
	C2	-8.7	2121	**Chain B**: ILE463 GLY464 SER465 GLY466 SER467 VAL471 ALA481 VAL482 LYS483 LEU514 ILE527 THR529 GLN530 TRP531 CYS532 GLY534 SER535 SER536 PHE583 ASP594 PHE595 GLY596
	C3			**Chain A**: VAL511 ASN512 ASP555 ARG558 GLN559 ARG562 HIS585 ASN588 THR589 **Chain B**: ASP479 TRP531 GLU533 HIS585

Proteins	Pocket ID	Vina Score	Cavity volume (Å3)	Interacting amino acids
				GLU586 THR589
	C4	-8.3	1065	**Chain A**: PHE468 LYS483 ALA497 ASN500 GLU501 VAL504 LEU505 LEU567 ILE572 ILE573 HIS574 ARG575 GLY593 ASP594 GLY596 LEU597 THR599 TYR633
	C5	-5	309	**Chain B**: LEU674 SER675 LEU678 ALA694 LEU697 LYS698 LYS699
P53	C1	-6.6	470	**Chain A**: THR102 GLN104 PHE109 ARG110 LEU111 GLY112 PHE113 TYR126 PRO128 ALA129 ASN131 TRP146 ASN268 SER269
	C2	-6.3	215	**Chain A**: VAL197 GLU198 GLY199 LEU201 ARG202 VAL218 PRO219 GLU221 PRO222 PRO223 CYS229 THR230 THR231 ILE232 HIS233
	C3	-5.8	208	**Chain A**: LEU145 VAL157 VAL197 GLU198 GLY199 LEU201 VAL218 PRO219 TYR220 GLU221 PRO222 PRO223 CYS229 THR230 THR231 ILE232 HIS233
	C4	-6.8	127	**Chain A**: SER96 PRO98 SER99 ARG156 ARG158 MET160 LEU206 ASP208 THR211 ARG213 SER215 ILE254 THR256 GLU258 SER261 GLY262 ASN263 LEU264 ARG267
	C5	-4.3	101	**Chain A**: VAL147 ASP148 SER149 THR150 TYR220 PRO222 PRO223 GLU228
BSA	C1	-6.5	8389	**Chain A**: ARG194 ARG217 GLN220 LYS221 ALA290 GLU291 VAL292 GLU293 LYS294 PRO338 GLU339 TYR340 ALA341 VAL342 ARG435 LYS439 GLU443 PRO446 CYS447 ASP450 TYR451
	C2	-7.1	3498	**Chain A**: ASP108 SER109 PRO110 ASP111 LEU112 LYS114 ARG144 PRO420 VAL423 GLU424 ARG427 ARG458 THR518 GLU519 ILE522
	C3	-5.8	1508	**Chain A**: PHE501 GLU503 LYS504 PHE506 THR507 PHE508 HIS509 PHE567 ALA568 GLY571 PRO572 VAL575
	C4	-6	793	**Chain A**: GLU100 LEU103 SER104 TYR147 CYS199 ILE202 GLN203 LYS204 LYS242 CYS245 HIS246
	C5	-6.6	356	**Chain A**: LEU386 GLN389 ASN390 GLN393 ALA405 VAL408 ARG409 ARG412 LYS413 SER488 ALA489 LEU490 THR491 PRO492

Table S9. For complex 3				
Proteins	**Pocket ID**	**Vina Score**	**Cavity volume (Å3)**	**Interacting amino acids**

VEGF	C1	-6.4	95	**Chain E**: MET138 TYR139 SER140 GLU141 PRO143 PHE172 LEU204 THR206 LEU215 TYR216 LYS217 ASN219
	C2	-5.5	84	**Chain E**: ILE165 THR166 VAL167 THR168 LEU169 THR176 LEU177 ILE178 PRO179 ASP180 GLY181 TRP186
	C3	-5.7	83	**Chain E**: ARG133 PRO134 THR161 SER162 ASN164 ILE165 THR166 THR210 VAL211 ASN212 TYR216
	C4	-5.7	77	**Chain E**: ARG133 PRO134 THR161 SER162 ASN164 ILE165 THR166 THR210 VAL211 ASN212
	C5	-6.3	73	**Chain E**: GLU144 ILE145 ILE146 HIS147 MET148 THR149 ARG152 GLU153 VAL155 PRO157 GLN225
TGFB1	C1	-6.8	126	**Chain A**: LEU20 TYR21 ILE22 ASP27 LEU28 TYR39 ALA41 ASN42 PHE43 CYS44 PRO80 LEU83 ASN103 MET104 ILE105 VAL106
	C2	-5.9	83	**Chain A**: PHE24 ARG25 TRP30 LYS31 TRP32 ILE33 HIS34 GLU35 PRO36 LYS37 TYR91 VAL92 GLY93
	C3	-6.1	56	**Chain A**: ASN14 GLY46 PRO47 CYS48 PRO49 TYR50 ASN66 GLN67 PRO70 GLY71 ALA72 SER73 ALA74 ALA75 PRO76
	C4	-5.7	49	**Chain A**: THR4 PHE8 GLN19 PRO36 GLY38 TYR39 HIS40 ASN42 LEU86 PRO87 ILE105 ARG107
	C5	-6.4	44	**Chain A**: CYS7 PHE8 SER10 THR11 GLU12 LYS13 VAL17 ARG18 GLN19 PHE43 LEU45 GLY46
BRAF	C1	-9.6	2436	**Chain A**: ILE463 GLY464 VAL471 ALA481 LYS483 LEU514 THR529 GLN530 TRP531 CYS532 GLY534 SER535 SER536 HIS539 ASN580 PHE583 PHE595 LEU597
	C2	-8	2121	**Chain B**: SER467 ALA497 ASN500 GLU501 VAL504 LEU505 THR508 ILE513 LEU567 ILE572 ILE573 HIS574 ARG575 ASP576 GLY593 ASP594
	C3	-8.3	1855	**Chain A**: VAL511 ASN512 ASP555 GLN559 ARG562 HIS585 GLU586 ASN588 THR589 **Chain B**: ASP479 GLN530 TRP531 GLU533 HIS585 GLU586 ASN588 THR589
	C4	-8.6	1065	**Chain A**: GLN493 ALA497 ASN500 GLU501 VAL504 LEU505 LEU567 ILE572 ILE573 HIS574 ARG575 GLY593 ASP594 GLY596 THR599 TYR633
	C5	-5.3	309	**Chain B**: SER675 PRO676 LEU678 ALA694 LEU697 LYS698 LYS699 LYS700 GLU703
P53	C1	-7.8	413	**Chain B**: SER1742 ASP1743 LEU1745 ALA1746 SER1749 ARG1811 TYR1852 LEU1854 SER1943 GLN1944 GLU1945 GLN1949 LYS1964 TYR1969

	C2	-7.4	272	**Chain B**: LEU1931 LYS1932 ALA1934 GLU1935 GLN1938 LEU1939 PRO1940 VAL1941 PHE1959 LYS1960 TYR1965 LYS1966 HIS1967 ASP1968
	C3	-6	265	**Chain B**: PRO1769 PRO1770 PHE1771 ASP1807 SER1827 HIS1828 VAL1829 HIS1832 ASP1833 TYR1846 LEU1848 PRO1849
	C4	-6.3	187	**Chain B**: GLN1801 SER1821 GLY1822 PRO1824 TYR1843 ARG1844 LEU1847 TRP1862 PRO1864 ARG1865 GLU1866 ASN1867
	C5	-7.9	113	**Chain B**: THR1740 SER1742 ARG1811 PHE1816 PHE1884 THR1922 ASP1923 PRO1924 SER1943 GLN1944 GLU1945 ILE1948 LYS1964 LYS1966 HIS1967 TYR1969 VAL1970 SER1971
BSA	C1	-8.1	8389	**Chain A**: TYR149 GLU152 TYR156 GLU186 LYS187 THR190 SER191 ARG194 ARG198 TRP213 ARG217 ARG256 HIS287 ALA290 GLU291 TYR451
	C2	-9.9	3498	**Chain A**: LYS114 HIS145 ARG185 GLU186 LEU189 THR190 SER192 ALA193 GLU424 ARG427 SER428 LYS431 ARG435 TYR451 LEU454 ILE455 ARG458 THR518 ILE522
	C3	-6.8	1508	**Chain A**: PHE501 GLU503 LYS504 PHE506 THR507 PHE508 HIS509 PHE567 ALA568 GLY571 PRO572 VAL575
	C4	-6.7	793	**Chain A**: GLU100 LEU103 SER104 TYR147 ARG196 ILE202 GLN203 LYS204 GLU207 LYS242 CYS245 HIS246
	C5	-7.7	356	**Chain A**: ASN385 LEU386 GLN389 ASN390 GLN393 LEU406 VAL408 ARG409 TYR410 ARG412 LYS413 SER488 LEU490 THR491 PRO492

Table S10. For complex 4				
Proteins	**Pocket ID**	**Vina Score**	**Cavity volume (Å3)**	**Interacting amino acids**
VEGF	C1	-6.7	95	**Chain E**: TYR139 SER140 GLU141 PRO143 LYS171 PHE172 PRO173 LEU174 ILE202 GLY203 LEU204 THR206 LYS217 ASN219 LEU221 THR222
	C2	-5.5	84	**Chain E**: PRO163 ILE165 THR166 VAL167 THR168 LEU169 THR176 LEU177 ILE178 PRO179 ASP180 GLY181 ILE184 ILE185 TRP186 ASP187 SER188
	C3	-3.9	83	**Chain E**: ARG133 THR161 SER162 ASN164 ILE165 THR166 THR210 VAL211 ASN212 GLY213
	C4	-5.9	77	**Chain E**: PRO163 ASN164 ILE165 THR166 VAL167 THR168 LYS170 THR176 ILE178 PRO179 TRP186 SER188 PHE192 GLU208 ALA209 THR210 LEU215
	C5	-5.6	73	**Chain E**: GLU137 GLU144 ILE145 ILE146 HIS147 MET148 THR149 ARG152 GLU153 LEU154 VAL155 PRO157 ARG159 ARG189 LYS190 GLN225
TGFB1	C1	-6.2	126	**Chain A**: LEU20 TYR21 ILE22 LYS26 ASP27 LEU28 TYR39 ALA41 ASN42 PHE43 CYS44 CYS78 VAL79 PRO80 LEU83 ASN103 MET104 ILE105 VAL106
	C2	-5.2	83	**Chain A**: PHE24 ARG25 TRP30 LYS31 TRP32 ILE33 HIS34 GLU35 PRO36 LYS37 TYR91 GLY93
	C3	-6.9	56	**Chain A**: LYS13 ASN14 GLY46 PRO47 CYS48 PRO49 TYR50 ALA63 ASN66 GLN67 ASN69 PRO70 GLY71 ALA72 SER73 ALA74 ALA75 PRO76 CYS77 CYS78
	C4	-5	49	**Chain A**: THR4 ASN5 PHE8 GLN19 PRO36 GLY38 TYR39 HIS40 ASN42 GLU84 LEU86 PRO87 ILE105 ARG107
	C5	-5.1	44	**Chain A**: CYS7 PHE8 SER10 THR11 GLU12 LYS13 VAL17 ARG18 GLN19 LEU20 TYR21 PHE43 LEU45 GLY46 PRO47
BRAF	C1			**Chain A**: ILE463 GLY464 SER465 VAL471 ALA481 VAL482 LYS483 GLU501 LEU514 ILE527 THR529 GLN530 TRP531 CYS532 GLU533 GLY534 SER535 SER536 TYR538

				HIS539 ALA543 ASN580 PHE583 ASP594 PHE595 GLY596 LEU597
	C2	-6.4	2121	**Chain B**: ILE463 GLY464 SER465 GLY466 VAL471 ALA481 LEU514 THR529 GLN530 TRP531 CYS532 GLY534 SER535 SER536 TYR538 HIS539 ASN580 PHE583 PHE595 GLY596
	C3	-5.1	1855	**Chain A**: ASP479 TRP531 GLU533 HIS585 GLU586 ASP587 ASN588 THR589 Chain B: LYS551 ASP555 ARG558 GLN559 ARG562 GLU586 ASN588 THR589
	C4	-6.9	1065	**Chain A**: PHE468 THR491 GLN493 GLN494 ALA497 ASN500 GLU501 VAL504 ILE573 HIS574 ARG575 ASP576 LYS578 ASP594 GLY596 LEU597 ALA598 THR599 SER614 TYR633
	C5	-5	309	**Chain B**: LEU674 SER675 PRO676 ASP677 LEU678 LYS687 LYS690 ARG691 ALA694 GLU695 LEU697 LYS698 LYS699
P53	C1	-7.1	470	**Chain A**: THR102 GLN104 PHE109 ARG110 LEU111 GLY112 PHE113 LEU114 HIS115 TYR126 PRO128 ALA129 ASN131 GLN144 TRP146 ASN268 SER269
	C2	-5.3	215	**Chain A**: LEU145 VAL157 GLY199 LEU201 ARG202 VAL218 PRO219 TYR220 GLU221 PRO222 PRO223 CYS229 THR230 THR231 ILE232
	C3	-6	208	**Chain A**: LEU145 THR150 PRO151 PRO152 PRO153 VAL157 VAL197 GLU198 GLY199 LEU201 ARG202 VAL218 PRO219 TYR220 GLU221 PRO222 PRO223 CYS229 THR230 THR231 ILE232 HIS233
	C4	-6.1	127	**Chain A**: SER95 SER96 VAL97 PRO98 SER99 LYS101 TYR103 ARG158 MET160 LEU206 ASP208 THR211 ARG213 SER215 THR256 GLU258 SER261 GLY262 ASN263 LEU264 ARG267
	C5	-4.5	101	**Chain A**: TRP146 VAL147 ASP148 SER149 THR150 PRO151 PRO152 PRO153 TYR220 GLU221 PRO222 PRO223 GLU228

BSA	C1			**Chain A**: TYR156 LYS187 THR190 SER191 ARG194 ARG198 TRP213 ARG217 GLN220 LYS221 HIS287 ALA290 GLU291 VAL292 GLU293 LYS294 PRO338 GLU339 TYR340 ALA341 VAL342 ARG435 LYS439 GLU443 PRO446 CYS447 ASP450 TYR451
		-7.5	8389	
	C2			**Chain A**: ASP108 SER109 PRO110 ASP111 LEU112 PRO113 LYS114 ARG144 HIS145 PRO146 ARG185 GLU186 LEU189 THR190 SER192 ALA193 ARG196 PRO420 GLU424 SER428 LYS431 ARG435 TYR451 LEU454 ILE455 ARG458 GLU519 ILE522
		-10.2	3498	
	C3			**Chain A**: PHE501 GLU503 LYS504 PHE506 THR507 HIS509 GLU564 PHE567 ALA568 GLY571 PRO572 VAL575 VAL576 GLN579
		-5.2	1508	
	C4			**Chain A**: PRO96 GLU100 SER104 HIS105 LYS106 ASP108 TYR147 ARG196 ILE202 GLN203 LYS204 LYS242 CYS245 HIS246 GLU464 LYS465
		-6.2	793	
	C5			**Chain A**: GLU382 PRO383 ASN385 LEU386 GLN389 ASN390 GLN393 VAL408 ARG409 ARG412 LYS413 ARG484 PRO485 PHE487 SER488 ALA489 LEU490 THR491 PRO492 GLU540
		-6.8	356	