Electronic Supplementary Material (ESI)

Metallo-Hydrazones of Pyridine–Thiophene Derivatives: Structure–Function Insight and Anticancer Evaluation of Co(III), Ni(II), Cu(II), and Zn(II) Complexes

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1. I.R. Spectra
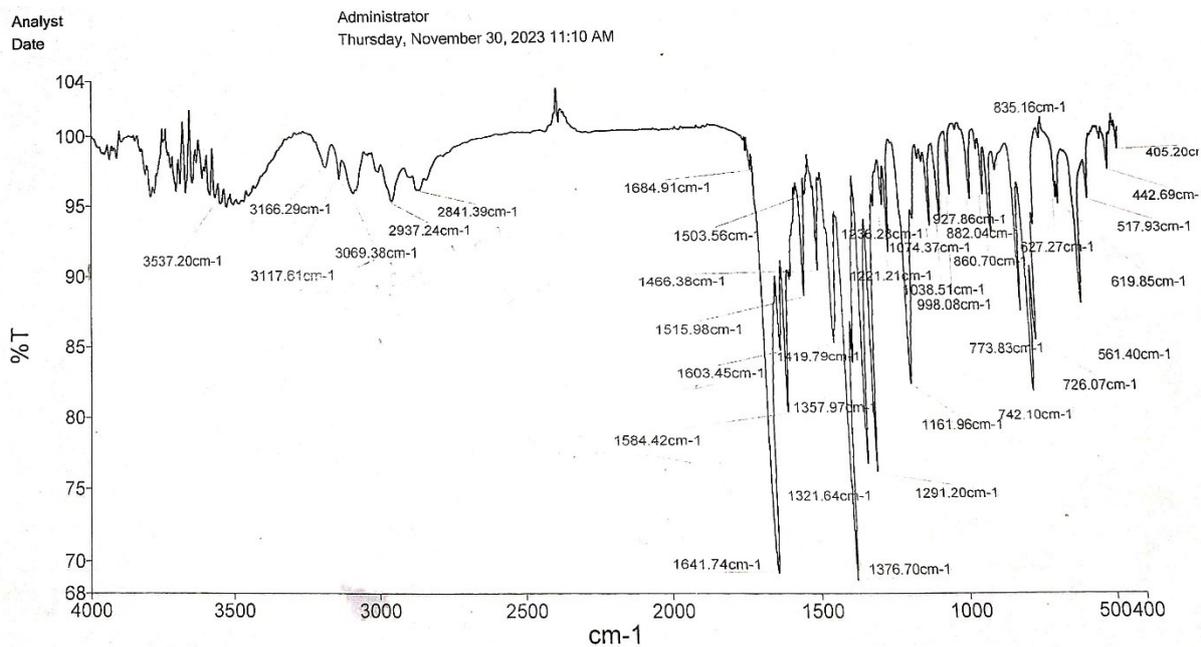
Fig. S1. IR spectrum of ligand **Hptch**.

Fig. S2. IR spectrum of complex **1**.

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Fig. S3. IR spectrum of complex **2**.

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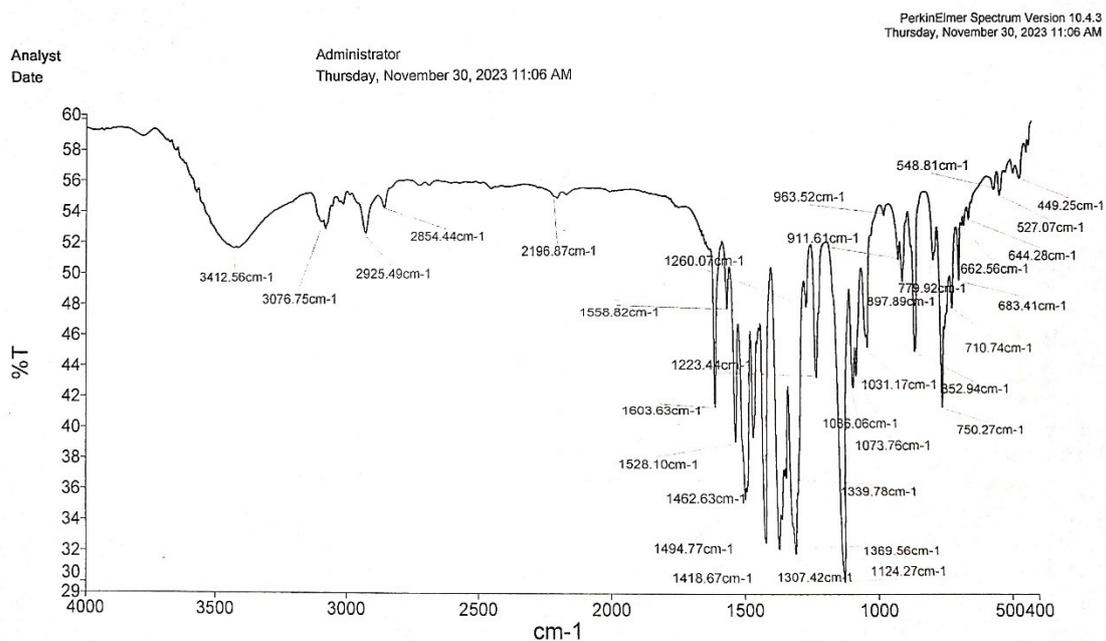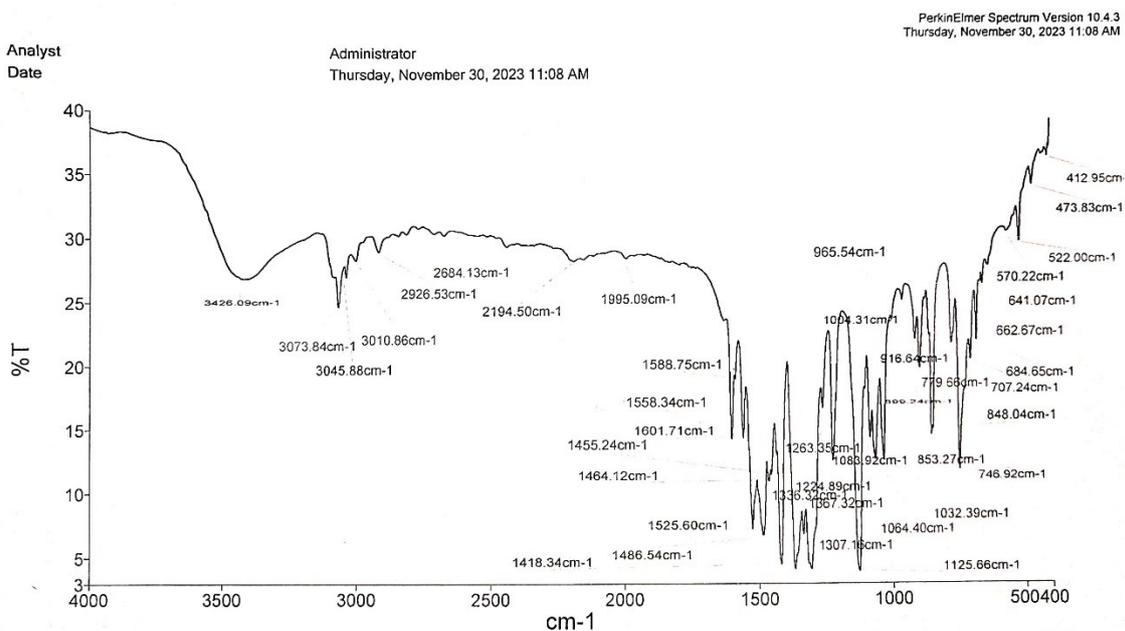
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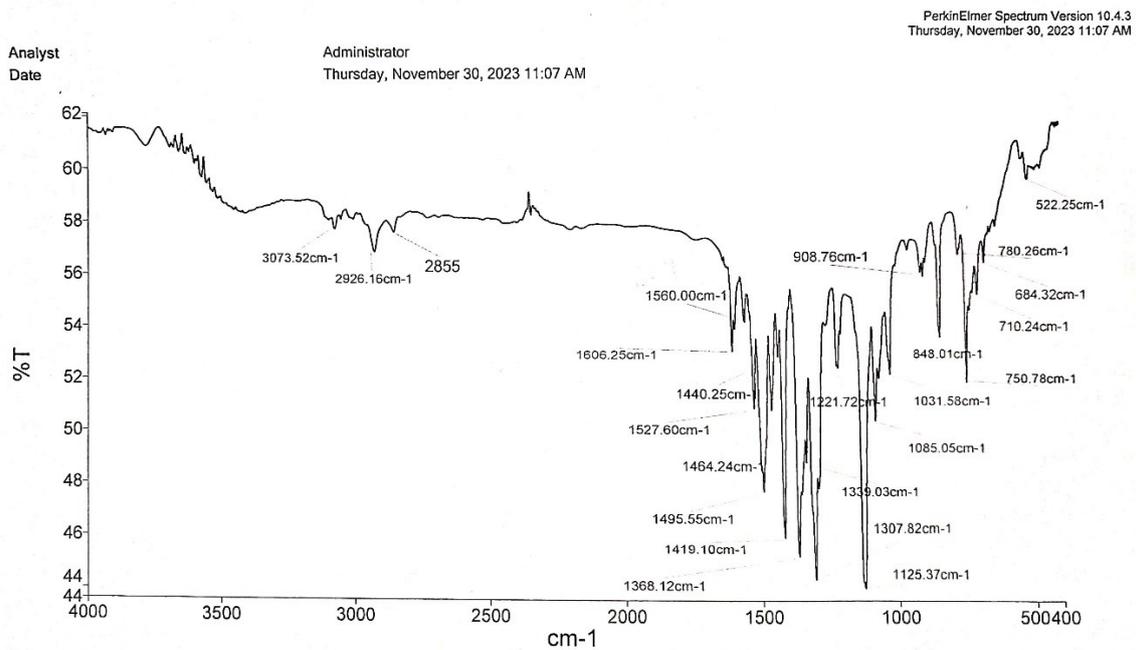
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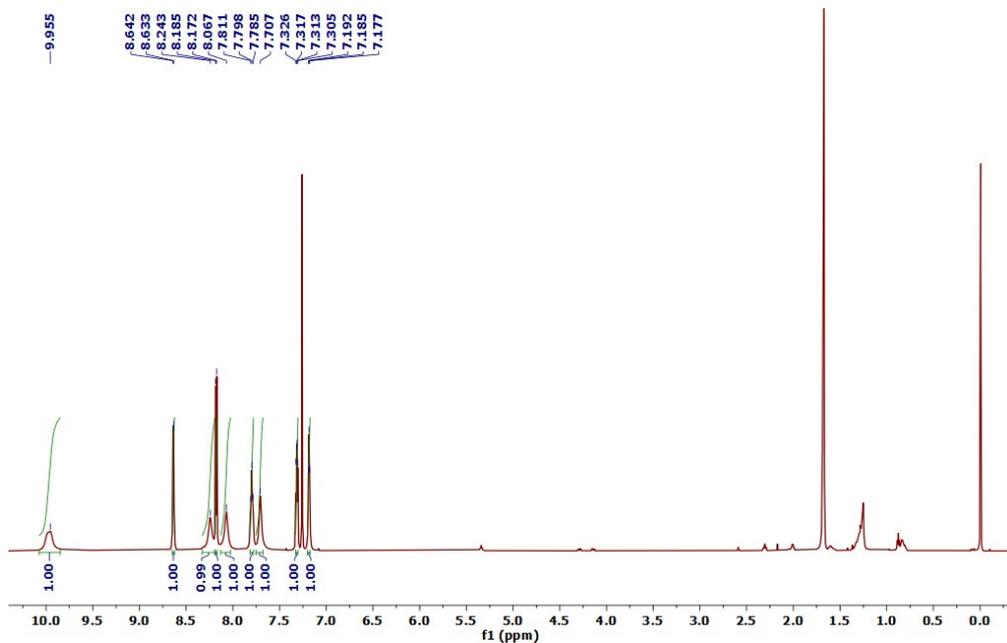## 2. NMR spectra

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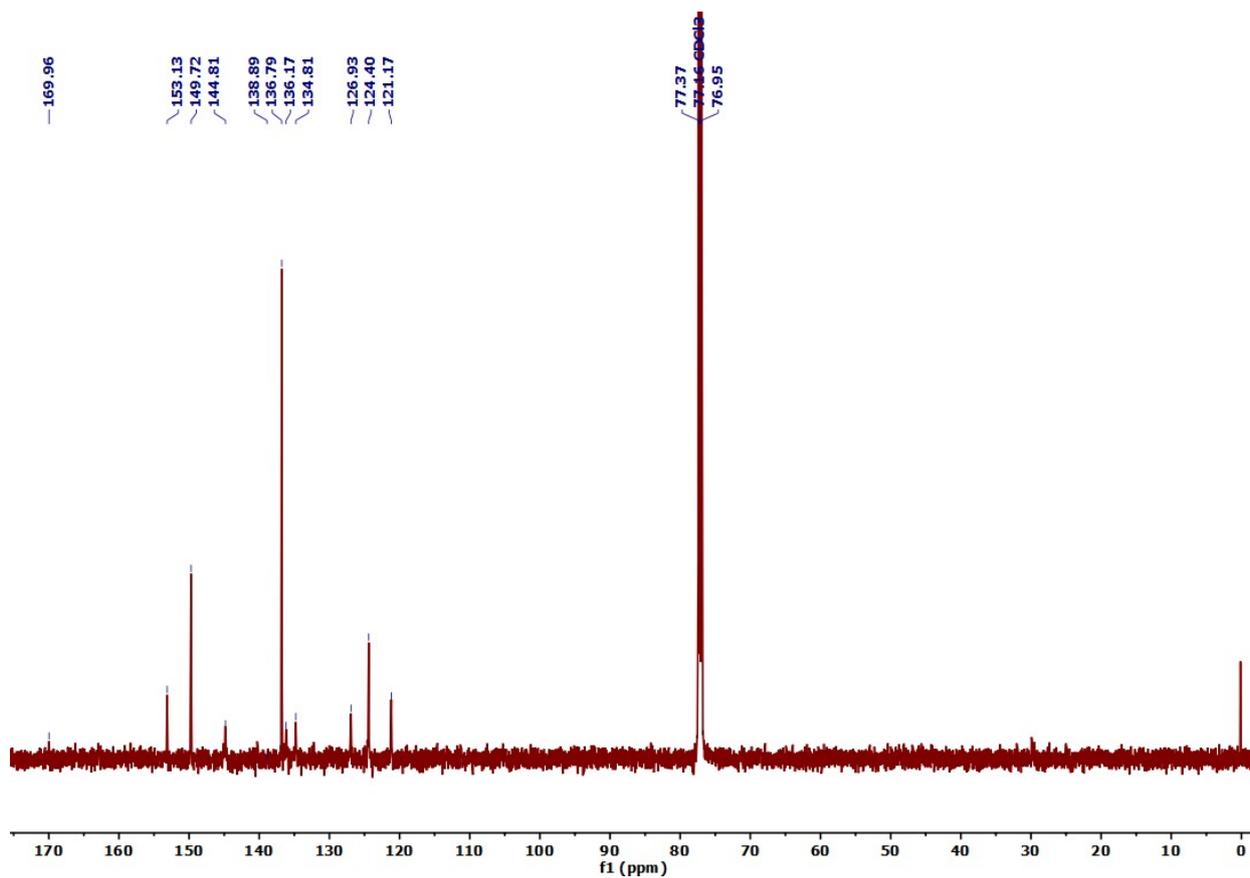
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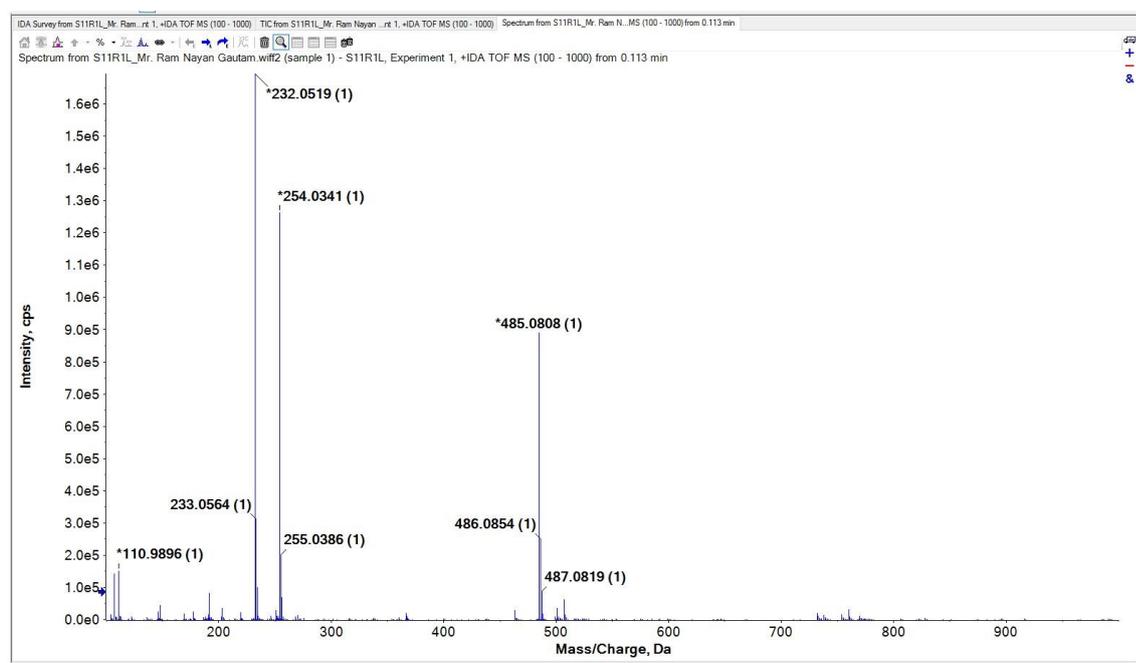
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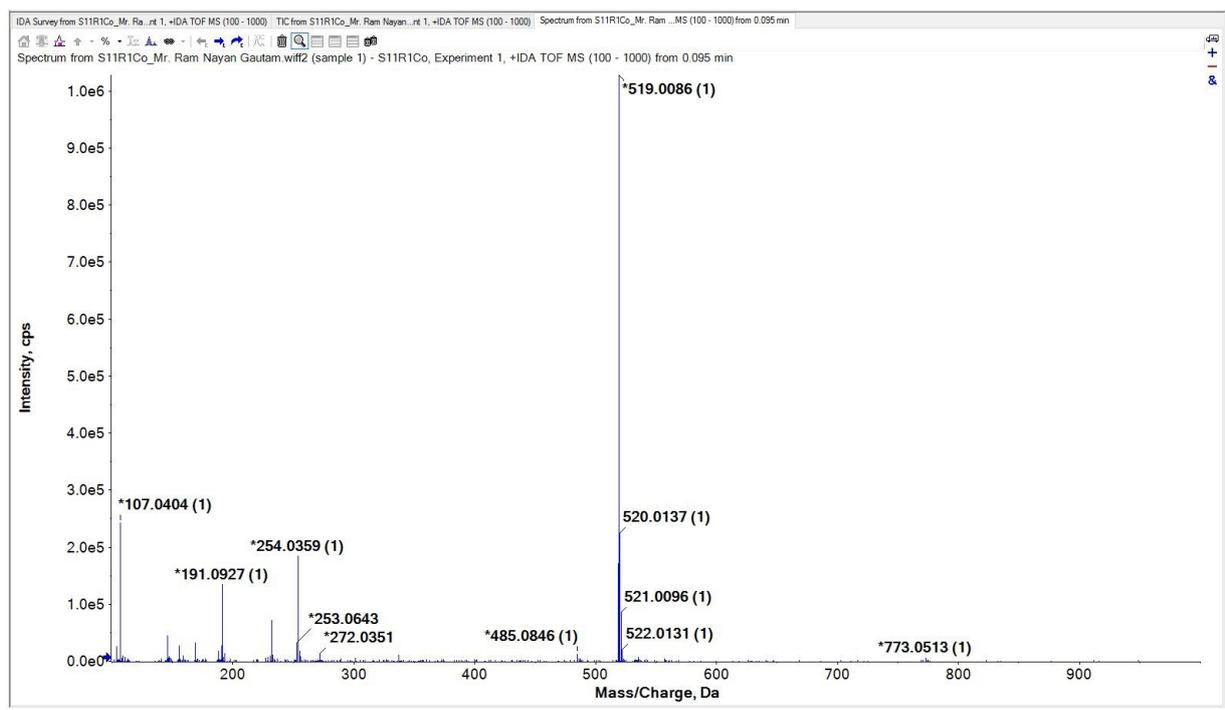

Fig. S8. HR-MS spectrum of ligand **Hptch**.
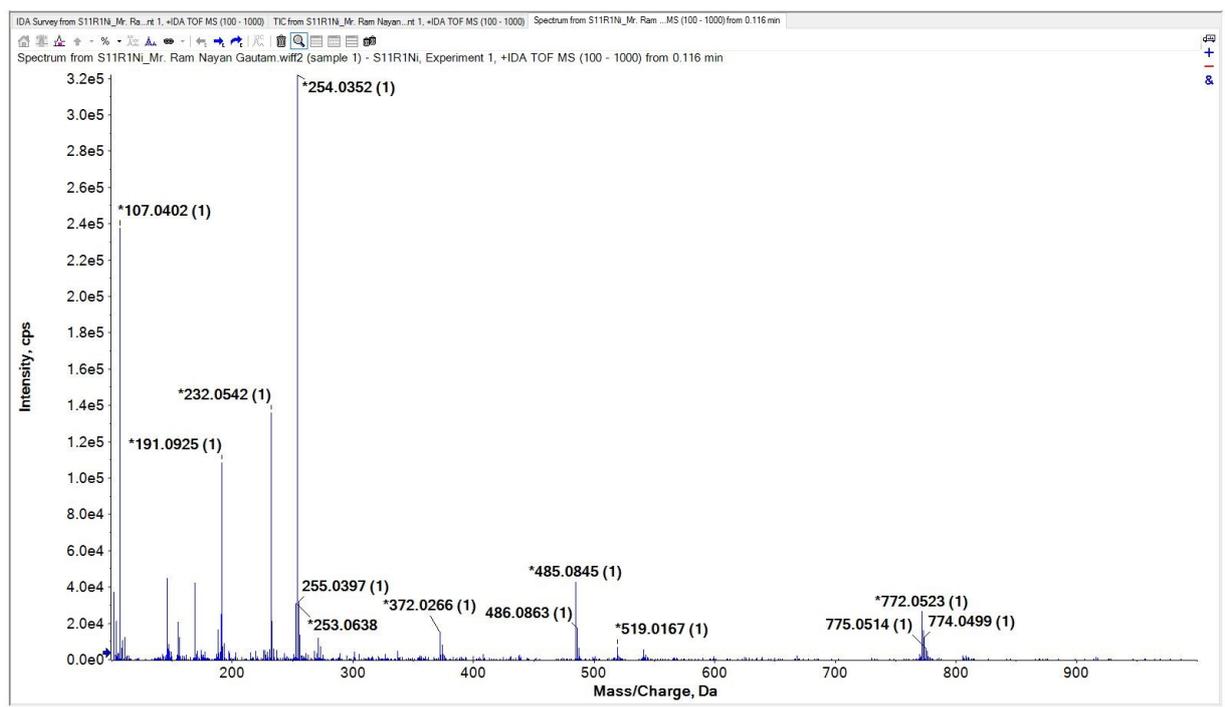
Fig. S9. HR-MS spectrum of complex **1**.

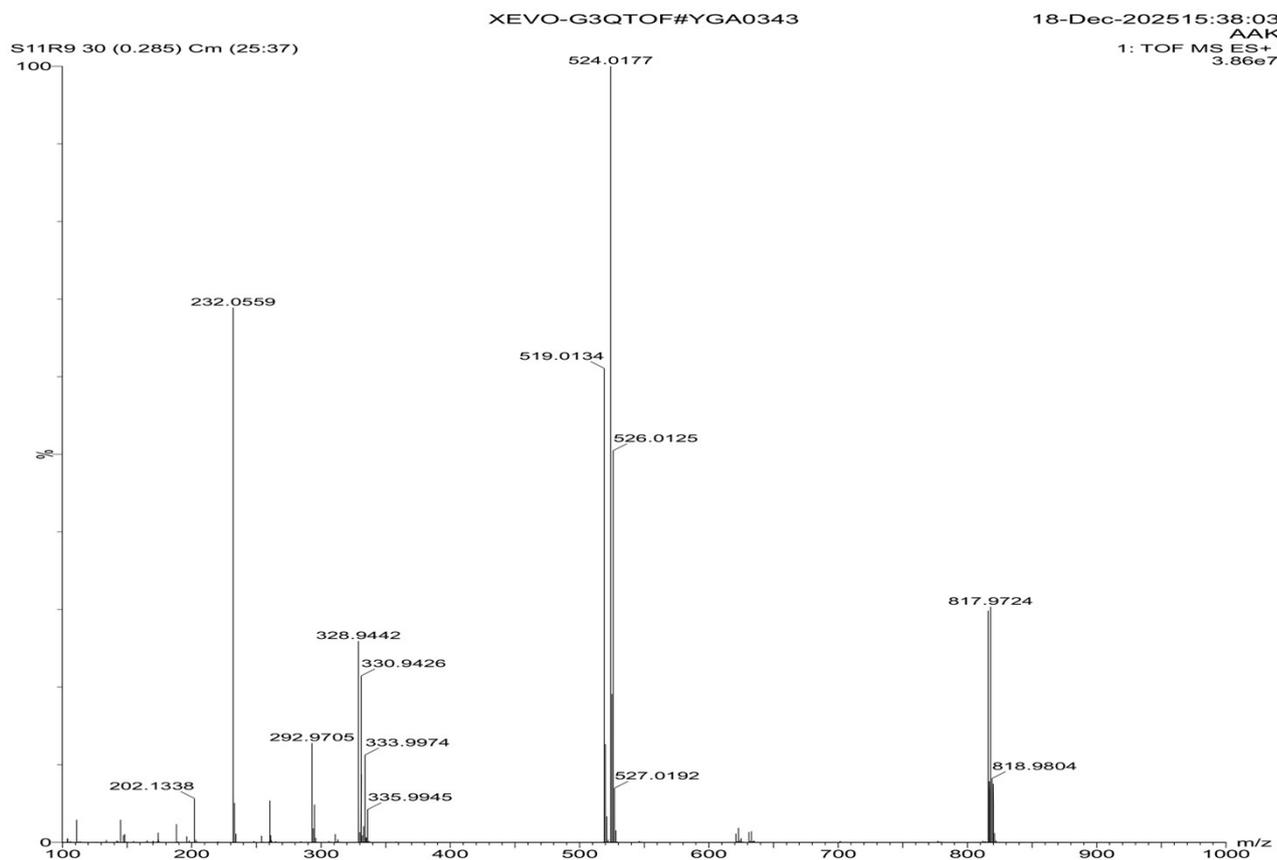**Fig. S10**. HR-MS spectrum of complex **2**.
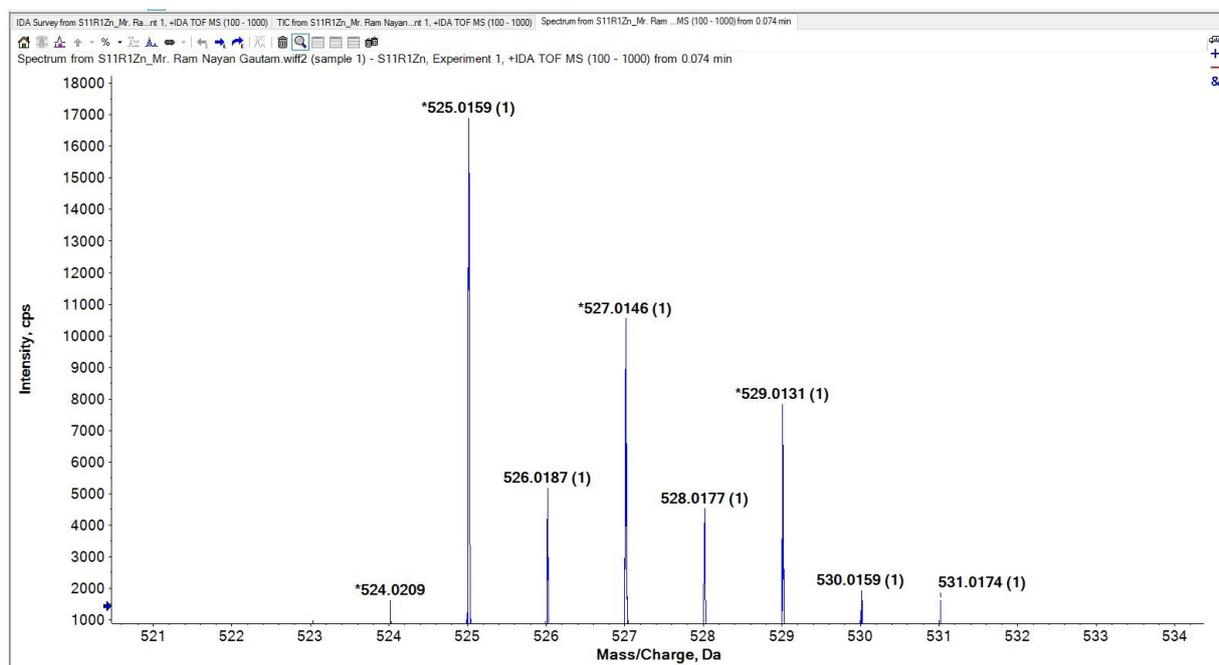
Fig. S11. HR-MS spectrum of complex **3**.

Fig. S12. HR-MS spectrum of complex **4**.

4. Crystallographic data

Table S1. Bond lengths [Å] and angles [°] for **Hptch**

Bond lengths [Å]		Bond angles [°]	
S(1)-C(5)	1.699(4)	C(5)-S(1)-C(2)	91.5(2)
S(1)-C(2)	1.726(4)	C(6)-N(2)-N(1)	115.6(3)
N(2)-C(6)	1.271(5)	C(1)-N(1)-N(2)	122.7(3)
N(2)-N(1)	1.374(4)	C(1)-N(1)-H(1)	122(3)
O(1)-C(1)	1.220(4)	N(2)-N(1)-H(1)	115(3)
N(1)-C(1)	1.351(5)	C(7)-N(3)-C(11)	117.9(3)
N(3)-C(7)	1.342(5)	O(1)-C(1)-N(1)	119.4(3)
N(3)-C(11)	1.343(6)	O(1)-C(1)-C(2)	120.4(4)

Table S2. Hydrogen bonds for **Hptch** [Å and °].

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(5)-H(5)···O(1)#1	0.93	2.54	3.161(6)	124.5
N(1)-H(1)···N(3)#2	0.91(4)	2.13(4)	3.037(5)	177(4)

Symmetry transformations used to generate equivalent atoms: #1 -x+3/2,y+1/2,z+1/2   #2 -x+1,-y+1,z-1/2

Table S3. Bond lengths [Å] and angles [°] for **Complex 1**

Bond lengths [Å]		Bond angles [°]	
Co(1)-O(1)	1.916(4)	N(2)-Co(1)-N(5)	176.3(3)
Co(1)-N(2)	1.842(6)	N(5)-Co(1)-O(2)	82.0(2)
Co(1)-N(1)	1.943(6)	N(5)-Co(1)-N(4)	82.2(3)
Co(1)-O(2)	1.925(5)	N(5)-Co(1)-O(1)	96.3(2)
Co(1)-N(5)	1.856(6)	N(2)-Co(1)-N(1)	82.6(3)
Co(1)-N(4)	1.943(6)	O(1)-Co(1)-N(4)	90.4(2)
N(3)-C(7)	1.326(9)	O(2)-Co(1)-N(1)	91.4(2)
O(1)-C(7)	1.290(8)	N(2)-Co(1)-N(4)	100.9(3)
N(2)-N(3)	1.373(9)	N(1)-Co(1)-N(4)	91.5(3)

Table S4. Bond lengths [Å] and angles [°] for **Complex 2**

Bond lengths [Å]		Bond angles [°]	
Ni(1)-O(1)	2.113(3)	N(2)-Ni(1)-N(5)	175.02(13)
Ni(1)-N(2)	1.999(3)	N(5)-Ni(1)-O(2)	76.52(11)
Ni(1)-N(1)	2.105(3)	N(5)-Ni(1)-N(4)	78.16(11)
Ni(1)-O(2)	2.093(3)	N(2)-Ni(1)-O(1)	76.28(11)
Ni(1)-N(5)	1.993(3)	N(2)-Ni(1)-N(1)	78.32(12)
Ni(1)-N(4)	2.131(3)	O(1)-Ni(1)-N(4)	92.48(11)
N(3)-C(7)	1.339(5)	O(2)-Ni(1)-O(1)	93.46(11)
O1-C7	1.268(4)	C(7)-O(1)-Ni(1)	109.7(2)
N2-N3	1.368(4)	C(6)-N(2)-Ni(1)	118.3(3)

Table S5. Bond lengths [Å] and angles [°] for **Complex 3**

Bond lengths [Å]		Bond angles [°]	
Cu(01)-O(1)	2.195(2)	N(2) -Cu(01)- N(5)	177.91(12)
Cu(01)-N(2)	1.962(3)	N(5)-Cu(01)-O(2)	77.17(11)
Cu(01)-N(3)	2.319(3)	N(5)-Cu(01)-N(6)	78.53(11)
Cu(01)-O(2)	2.111(2)	N(2)-Cu(01)-O(1)	76.02(10)
Cu(01)-N(5)	1.945(3)	N(2)-Cu(01)-N(3)	76.20(11)
Cu(01)-N(6)	2.150(3)	N(6)-Cu(01)-O(1)	90.13(10)
N(1)-C(1)	1.337(4)	O(2)-Cu(01)-N(3)	93.02(10)
C(1)-O(1)	1.257(4)	N(6)-Cu(01)-N(3)	92.99(11)
N(1)-N(2)	1.380 (4)	O(1)-Cu(01)-N(3)	151.99(10)

Table S6. Bond lengths [Å] and angles [°] for **Complex 4**

Bond lengths [Å]		Bond angles [°]	
Zn(01)-O(1A)	2.148(4)	N(2A)-Zn(01)-N(2B)	172.74(17)
Zn(01)-N(2A)	2.071(4)	N(2B)-Zn(01)-O(1B)	74.39(14)
Zn(01)-N(3A)	2.233(4)	N(2B)-Zn(01)-N(3B)	74.92(15)
Zn(01)-O(1B)	2.127(4)	N(2A)-Zn(01)-O(1A)	74.36(15)
Zn(01)-N(2B)	2.078(4)	N(2A)-Zn(01)-N(3A)	75.39(16)
Zn(01)-N(3B)	2.199(4)	O(1A)-Zn(01)-N(3B)	93.80(16)
N(1A)-C(5A)	1.338(7)	O(1B)-Zn(01)-N(3A)	93.91(15)
O(1A)-C(5A)	1.251(6)	N(2B)-Zn(01)-N(3A)	110.38(16)
N(2A)-N(1A)	1.358(6)	N(3B)-Zn(01)-N(3A)	92.27(15)

Table S7. Hydrogen bonds for **Complex 1** [Å and °].

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(1)-H(1A)···Cl(2)#1	0.93	2.96	3.538(11)	121.4
C(2)-H(2A)···Cl(2)#1	0.93	2.74	3.428(14)	131.5
C(11)-H(11A)···Cl(1)#2	0.93	2.84	3.641(8)	144.5
C(13)-H(13A)···Cl(1)#3	0.93	2.80	3.459(13)	128.7
C(15)-H(15A)···O(1W)#4	0.93	2.60	3.42(3)	147.5
C(21A^b)-H(21B^b)···S(1)#5	0.93	2.97	3.618(14)	128.4
O(1W)-H(1W2)···Cl(2)	0.82(2)	2.48(7)	3.18(2)	144(10)

Symmetry transformations used to generate equivalent atoms: #1 -x+1,y,-z+1/2   #2 x+1/2,-y+1/2,z+1/2

 #3 -x+3/2,y+1/2,-z+1/2 #4 -x+2,y,-z+1/2   #5 x-1,y,z

Table S8. Hydrogen bonds for **Complex 2** [Å and °].

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(1)-H(1A)···N(6)#1	0.93	2.57	3.249(5)	130.0
C(10^a)-H(10A^a)···O(2)#2	0.93	2.52	3.256(8)	136.2
C(11^a)H(11A^a) ···S(1^a)#3	0.93	2.75	3.605(7)	152.5
C(13)-H(13A)···N(3)#4	0.93	2.65	3.538(5)	161.1
C(17)-H(17A)···O(1)#5	0.93	2.63	3.361(4)	135.9
C(21^a)-H(21A^a)···O(2)#6	0.93	2.47	3.353(9)	159.4

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y,-z+1   #2 x,y+1,z   #3 -x+2,y+1/2,-z+3/2 #4 -x+2,-y+1,-z+1   #5 -x+1,-y+1,-z+1   #6 -x+1,y-1/2,-z+3/2

Table S9. Hydrogen bonds for **Complex 3** auto [Å and °].

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(3)-H(3)···Cl(2)#1	0.93	2.95	3.732(3)	142.4
C(14)-H(14)···Cl(3)#2	0.93	2.92	3.676(4)	138.8
C(19)-H(19)···S(1)#3	0.93	2.97	3.747(4)	142.7
C(8)-H(8)···O(2)#4	0.93	2.49	3.281(4)	142.6
C(5)-H(5)···O(1)#5	0.93	2.35	3.279(5)	177.7
C(23)-H(23)···S(2)	0.93	2.99	3.780(4)	138.1
C(23)-H(23)···N(4)	0.93	2.27	3.161(5)	150.6
C(10)-H(10)···Cl(3)#6	0.93	2.91	3.720(4)	145.8

Table S10. Hydrogen bonds for **Complex 4** auto [Å and °].

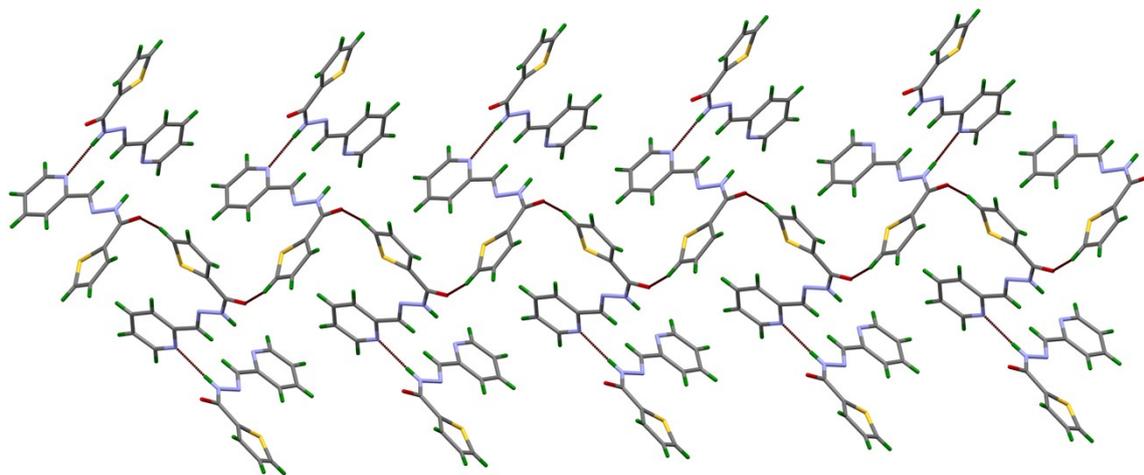| D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(11B)-H(11B)···N(1A)#1	0.93	2.57	3.289(7)	134.1
C(1B)-H(1B)···S(1B)#2	0.93	2.79	3.633(6)	151.8
C(2A)-H(2A)···O(1A)#3	0.93	2.51	3.400(8)	160.0

Fig. S13. Showing weak C-H···O intermolecular interactions leading to a wave-like architecture in the

Hptch.
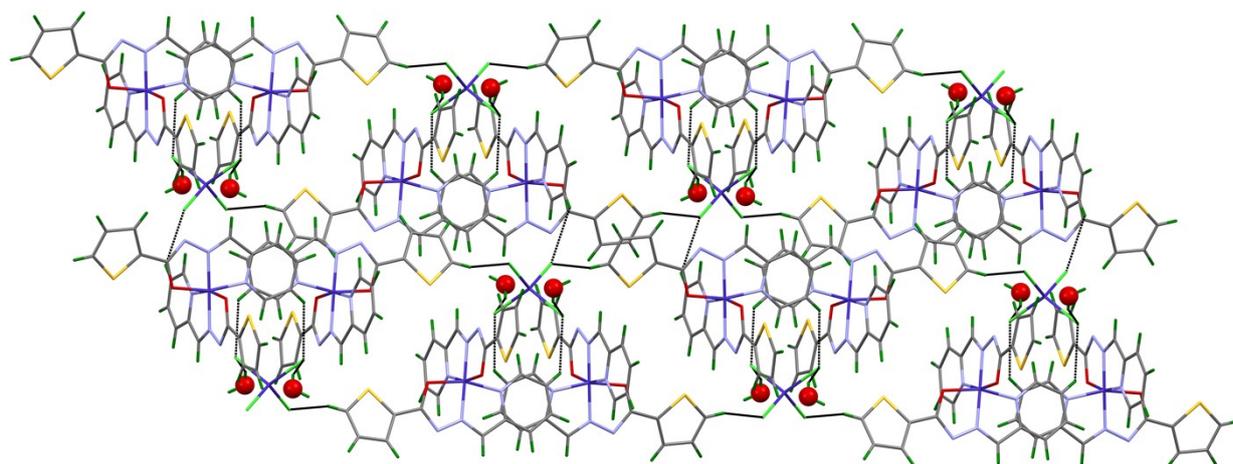
Fig. S14. Showing C-H···Cl interactions in Complex **1** leading to a paddle wheel-like

architecture (Oxygen atoms are presented in spacefill style)
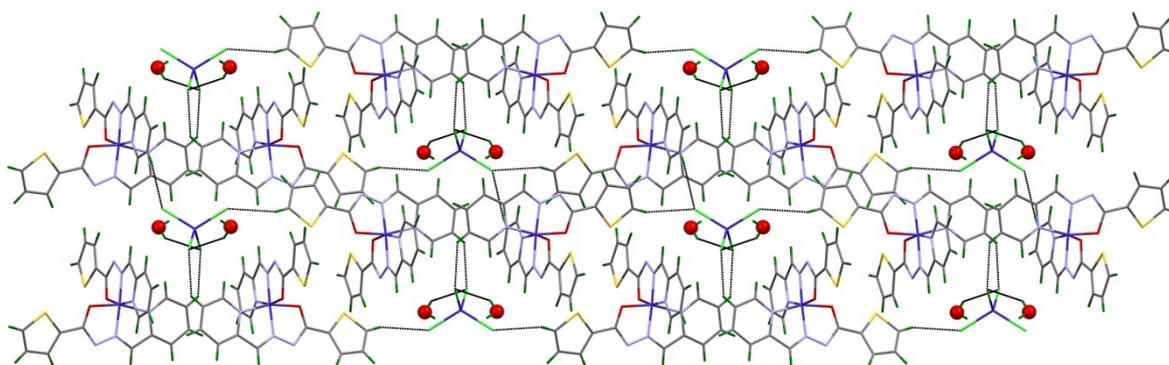
Fig. S15. Showing O-H···Cl and C-H···Cl interactions in Complex **1** leading to a supramolecular architecture.
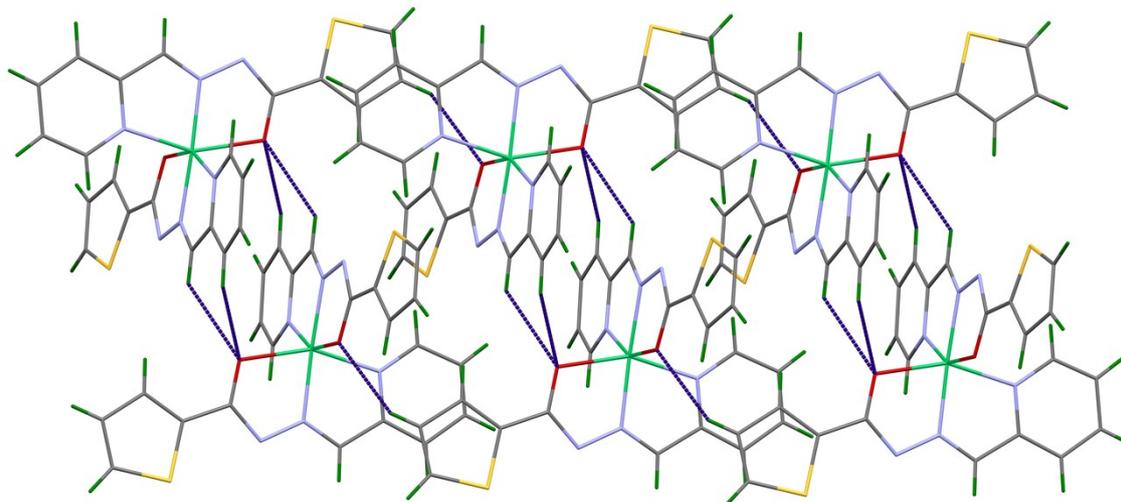
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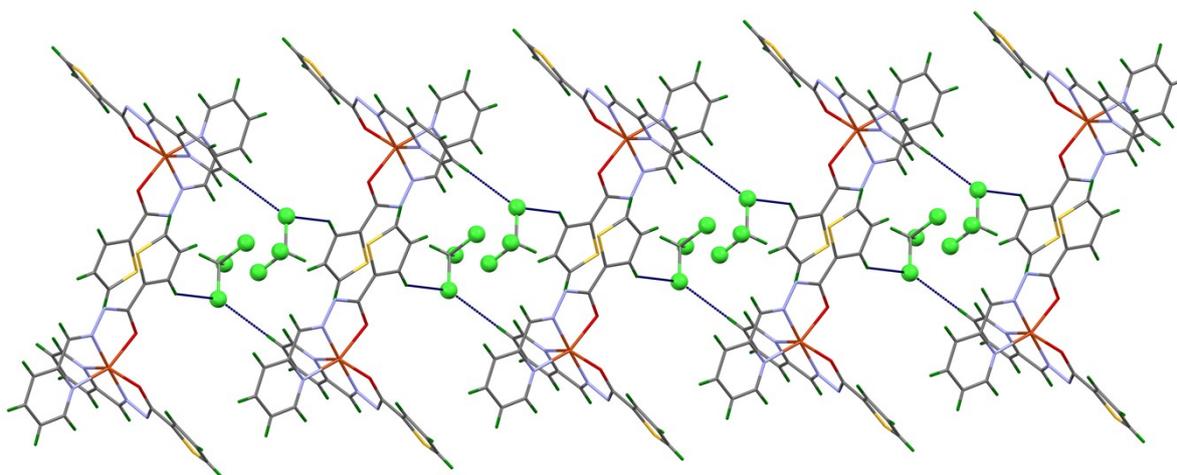
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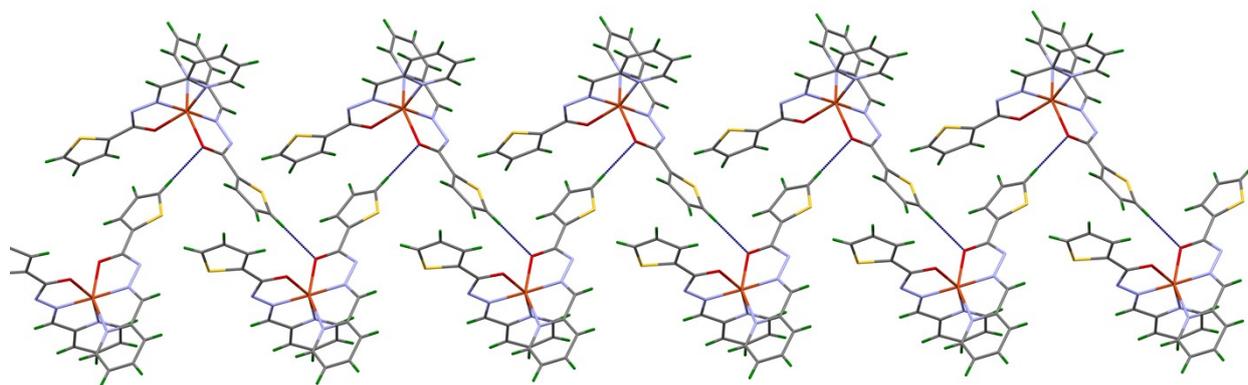
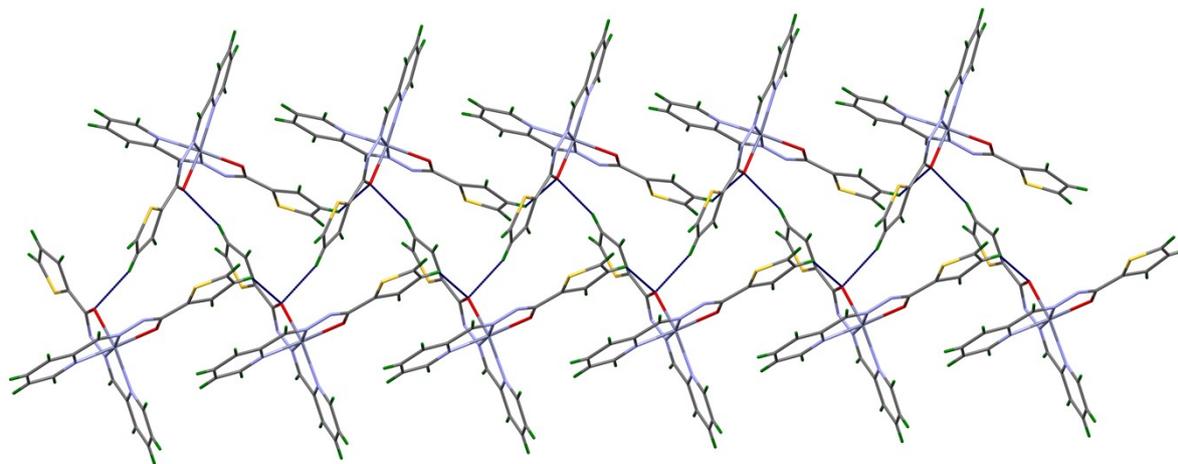**Fig. S18**. Showing CH⋯O interactions in Complex **3** leading to a linear chain structure.

Fig. S19. Showing CH⋯O interactions in Complex **4** leading to a wave-like architecture.

5. Molecular Docking
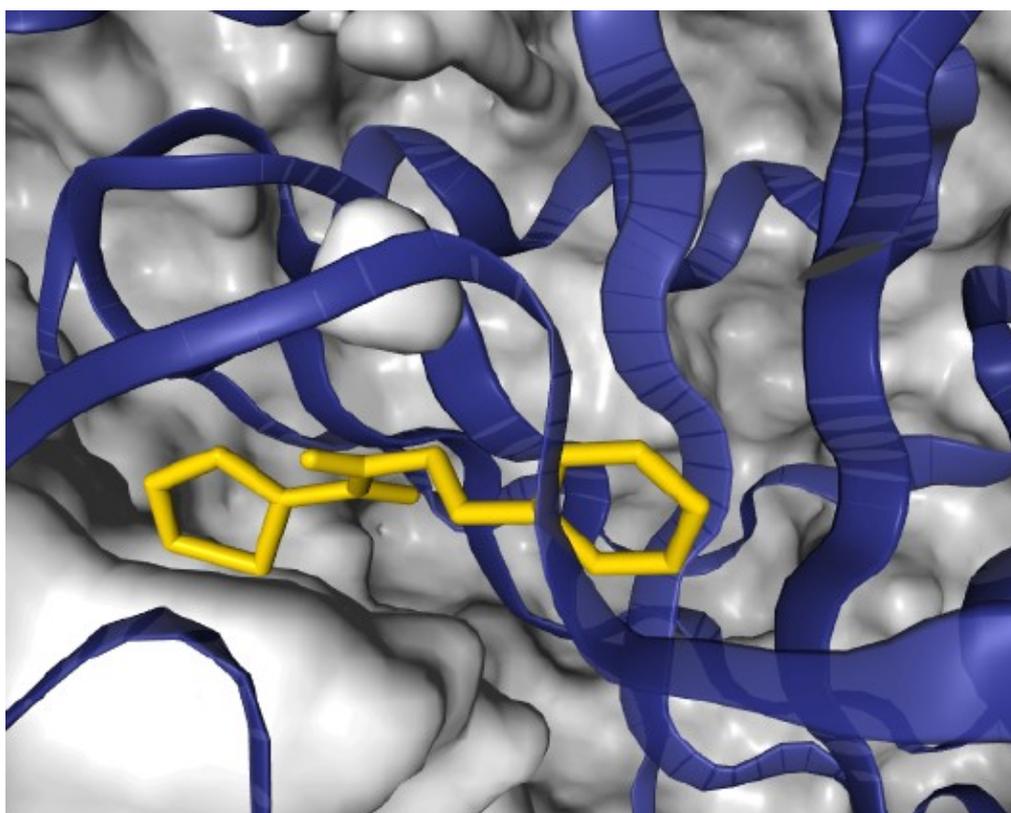
Fig. S20. Protein interaction of ligand **Hptch**.
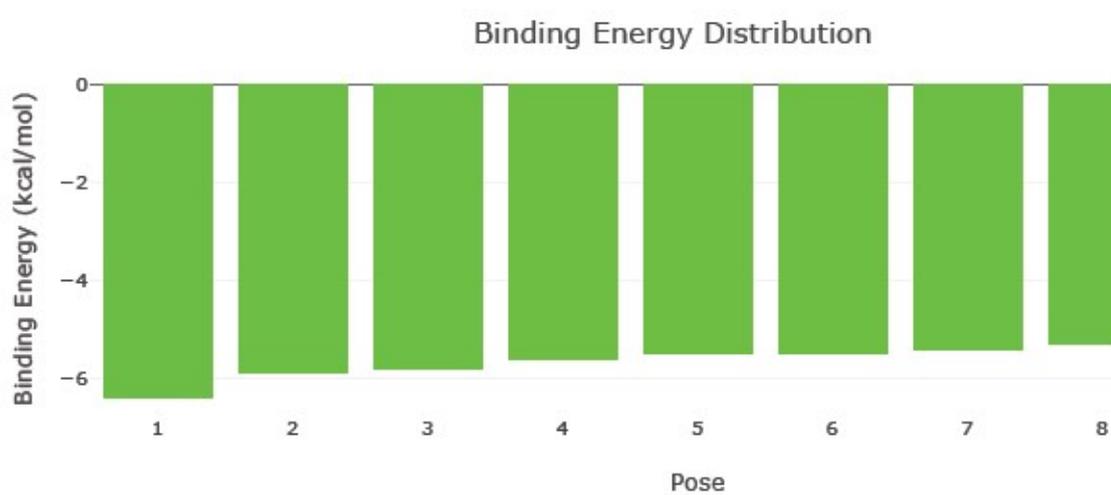
Fig. S21. Binding energy distribution of ligand **Hptch**.
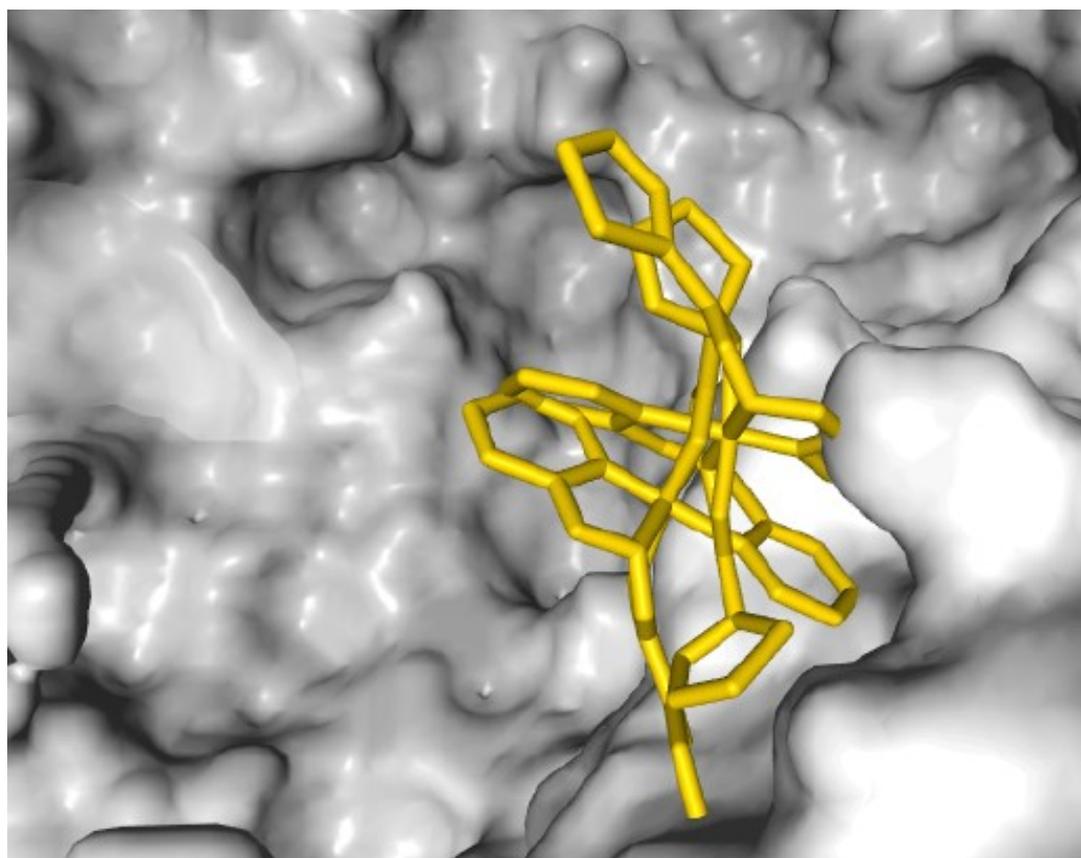
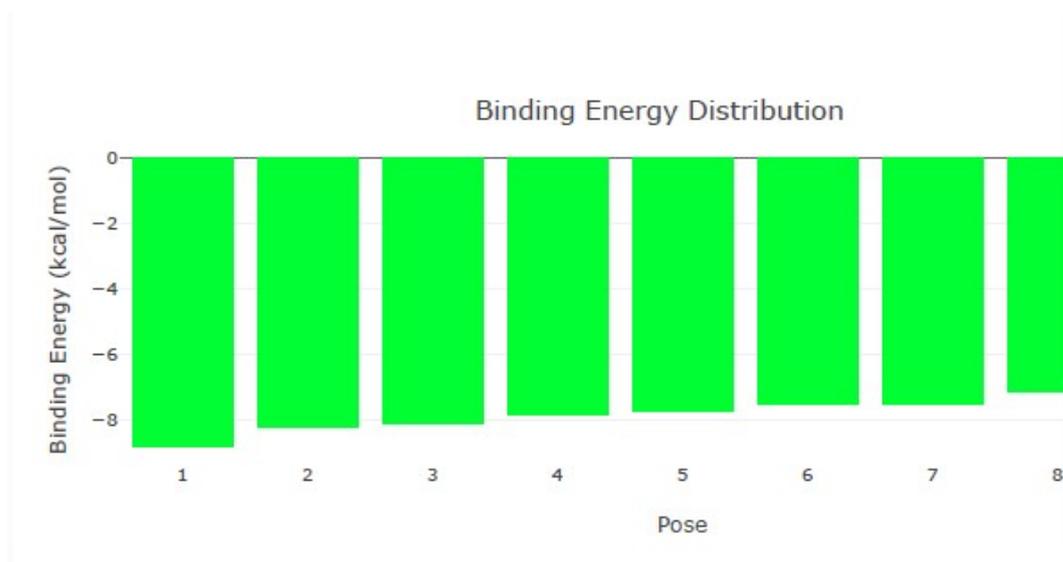**Fig. S22**. Protein interaction of complex **1**.
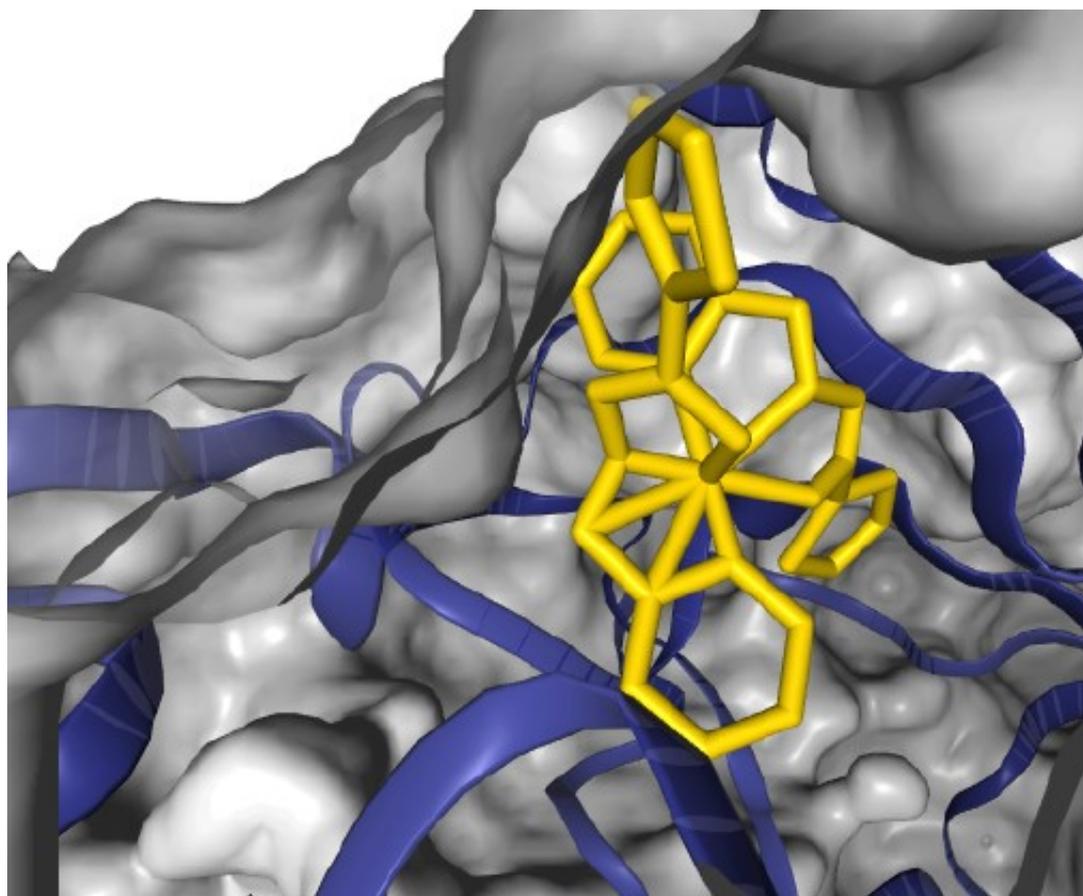

Fig. S23. Binding energy distribution of complex **1**.
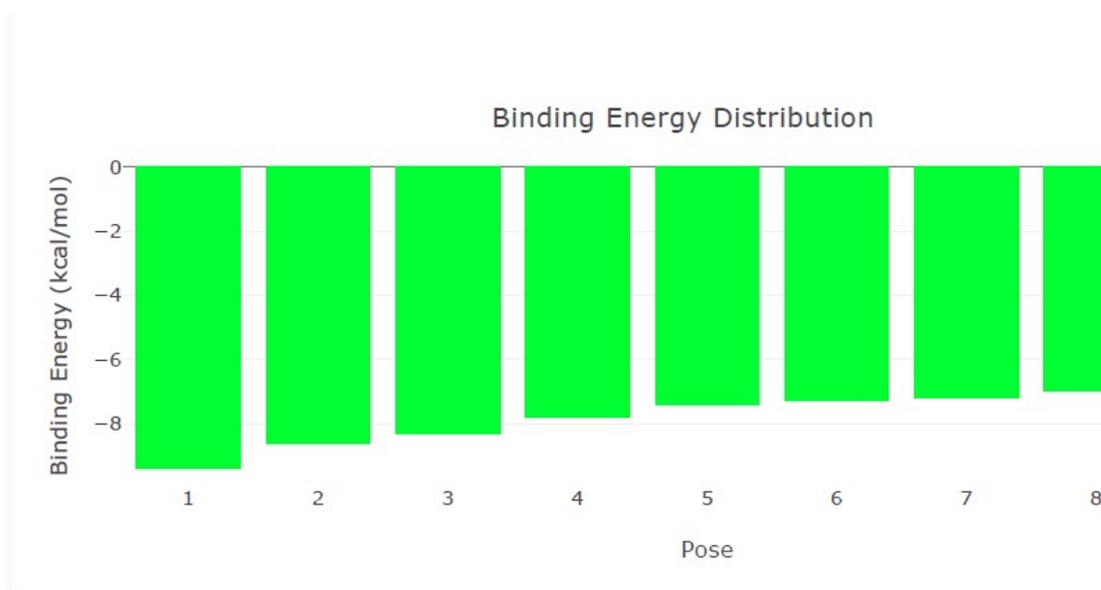
Fig. S24. Protein interaction of complex **2**.

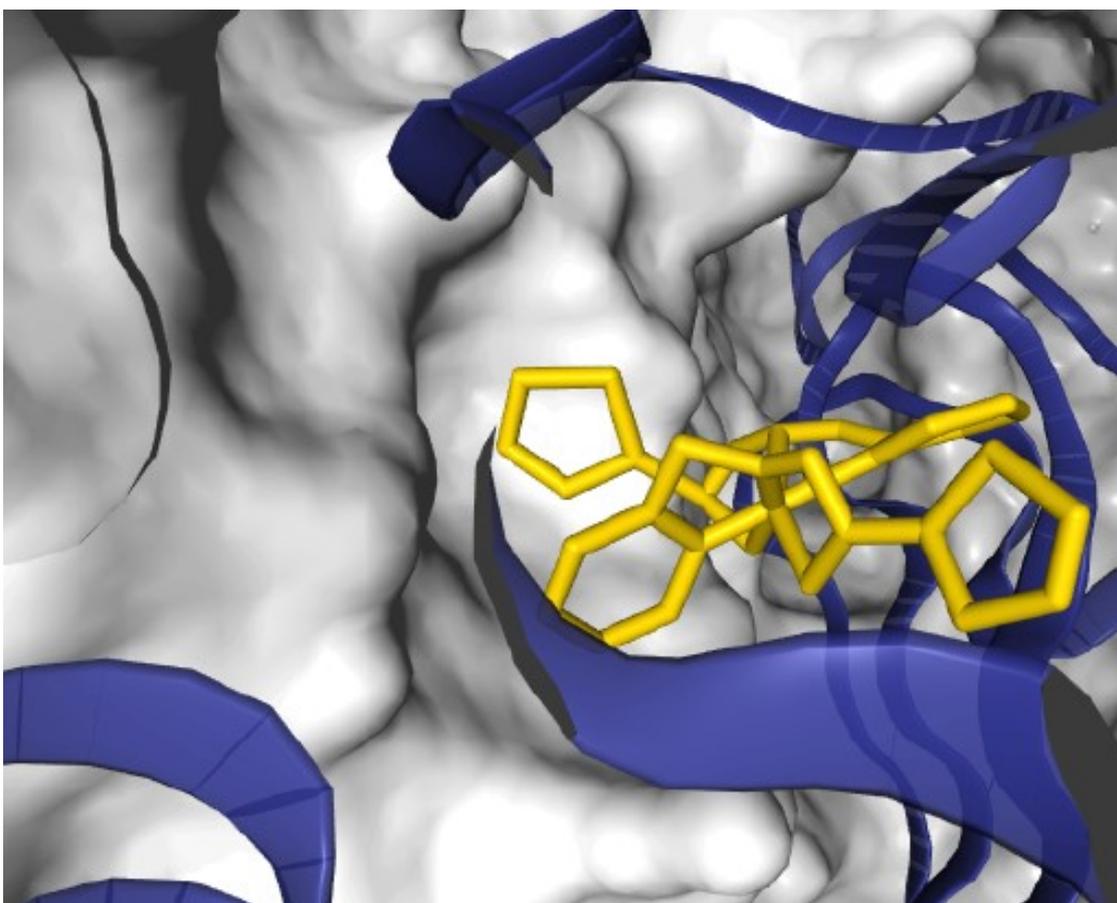**Fig. S25**. Binding energy distribution of complex **2**.
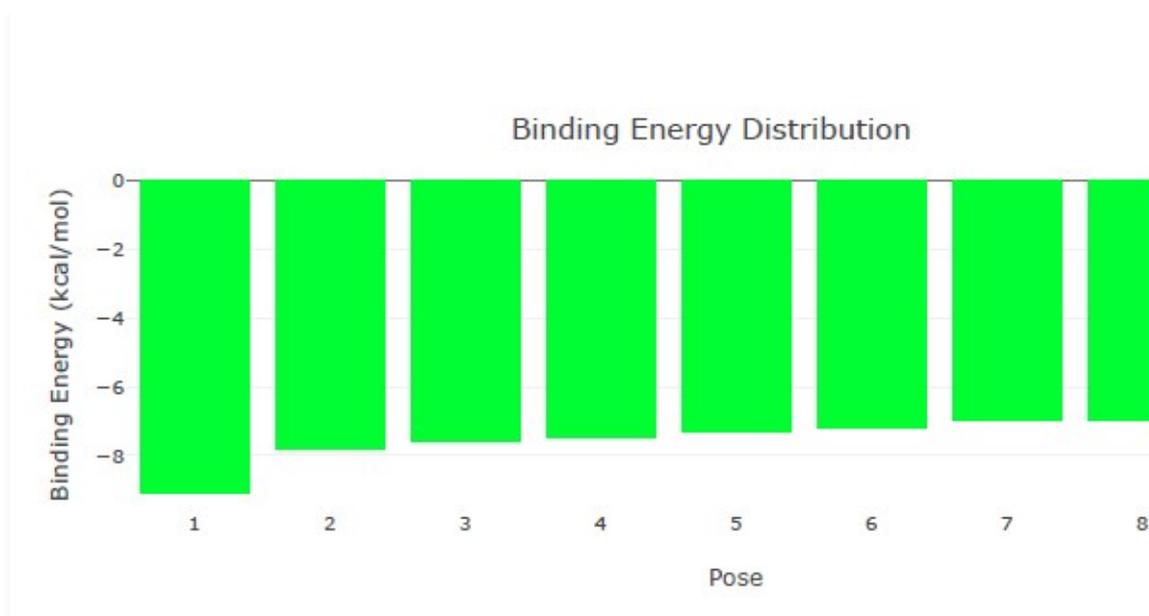
Fig. S26. Protein interaction of complex **3**.
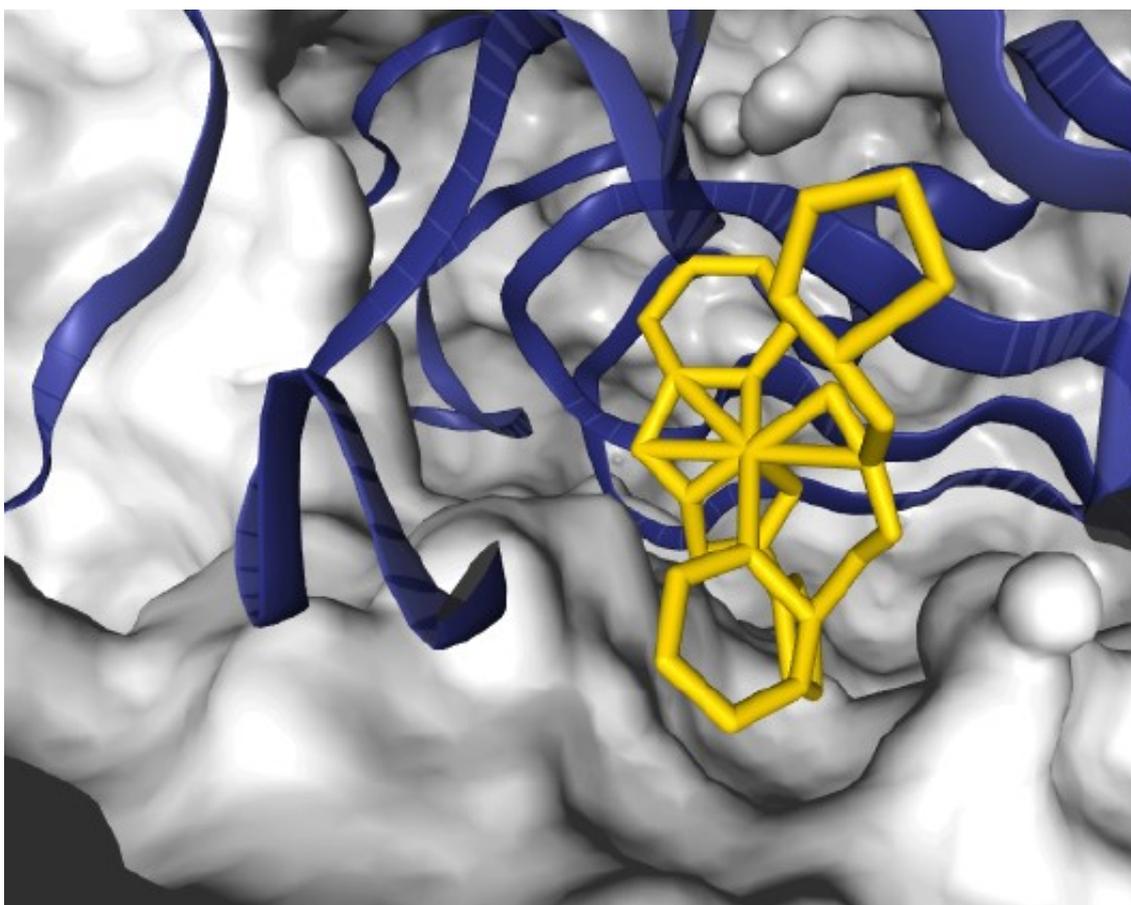

Fig. S27. Binding energy distribution of complex **3**.
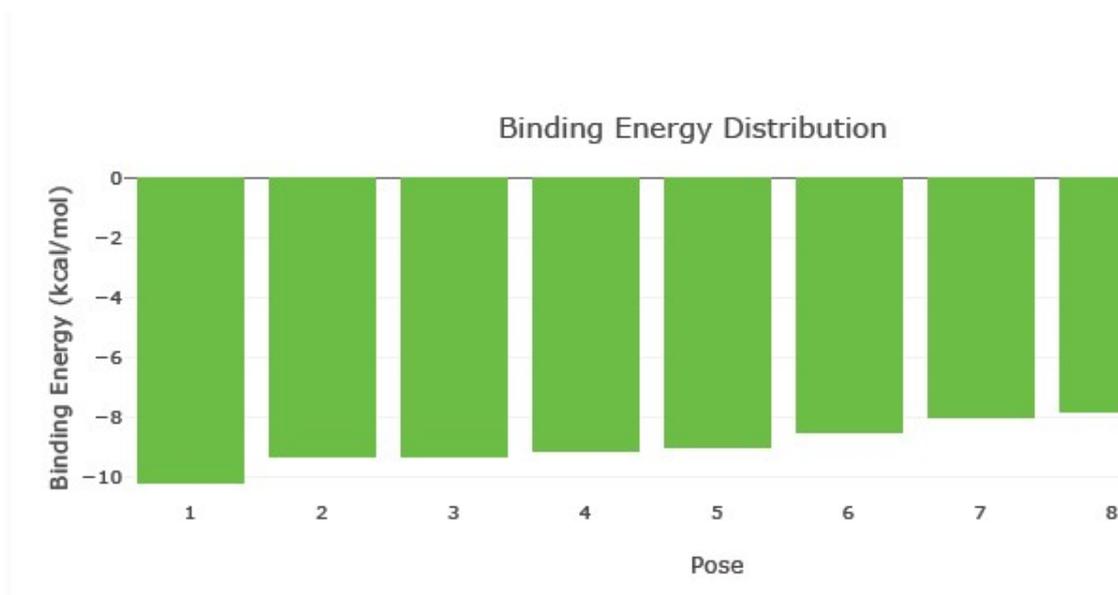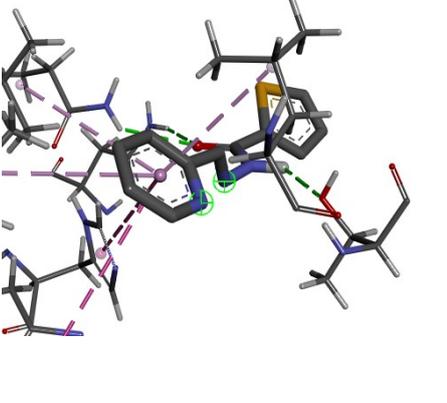
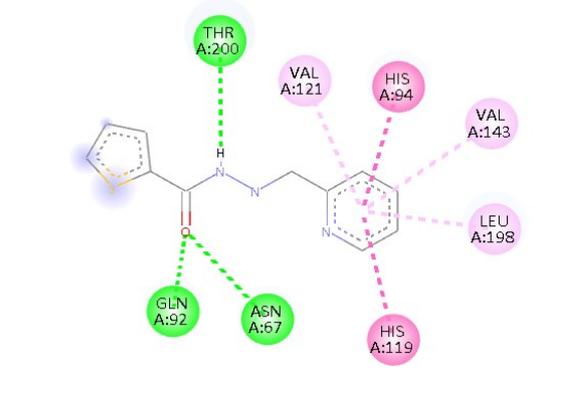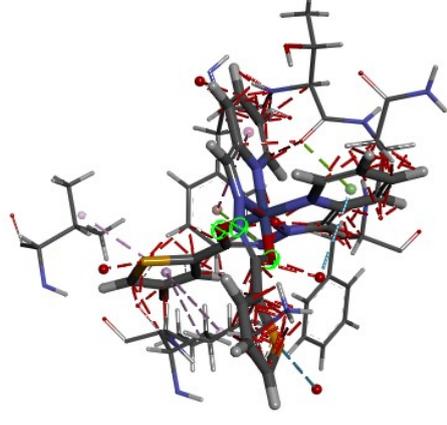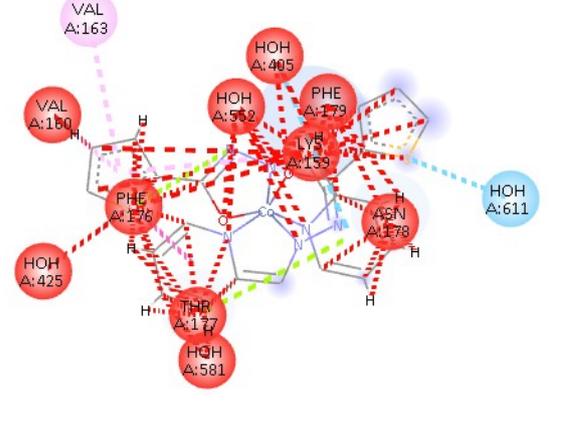**Fig. S28**. Protein interaction of complex **4**.

Fig. S29. Binding energy distribution of complex **4**.

Table S11: Receptor ligand interaction on a 2D diagrams.

Compound	Receptor-ligand interaction	Receptor-ligand interaction in a **2D**-diagram
Hptch		
Complex 1		
Complex 2		

Complex 3		
Complex 4		

Interactions

■ (red)	Unfavorable Bump	■ (pink)	Pi-Pi Stacked
■ (light blue)	Water Hydrogen Bond	■ (light pink)	Pi-Alkyl
■ (green)	Pi-Lone Pair		

Interactions

■ (red)	Unfavorable Bump	■ (pink)	Pi-Pi Stacked
■ (orange)	Pi-Cation	■ (light pink)	Pi-Alkyl
■ (green)	Pi-Lone Pair		