Revised Supplementary

Dithiocarbamate based novel anti-histaminic agents: Synthesis, characterization, crystal structure and thermal study

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1. FTIR Spectra:

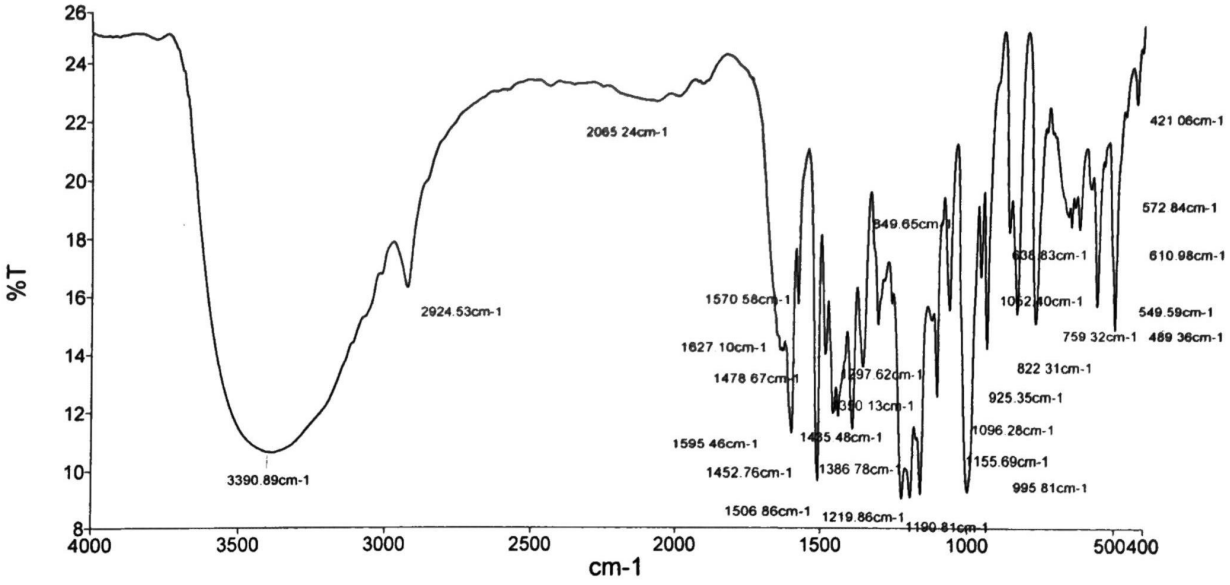

Fig. S1: FTIR spectra of ligand.

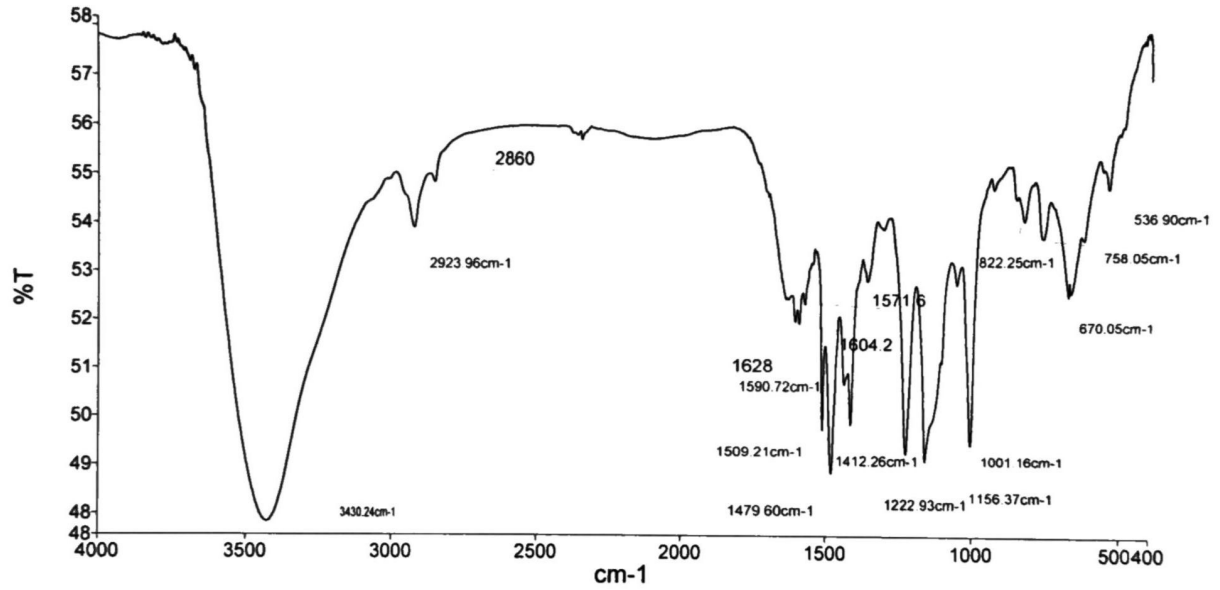

Fig. S2: FTIR spectra of complex 1.

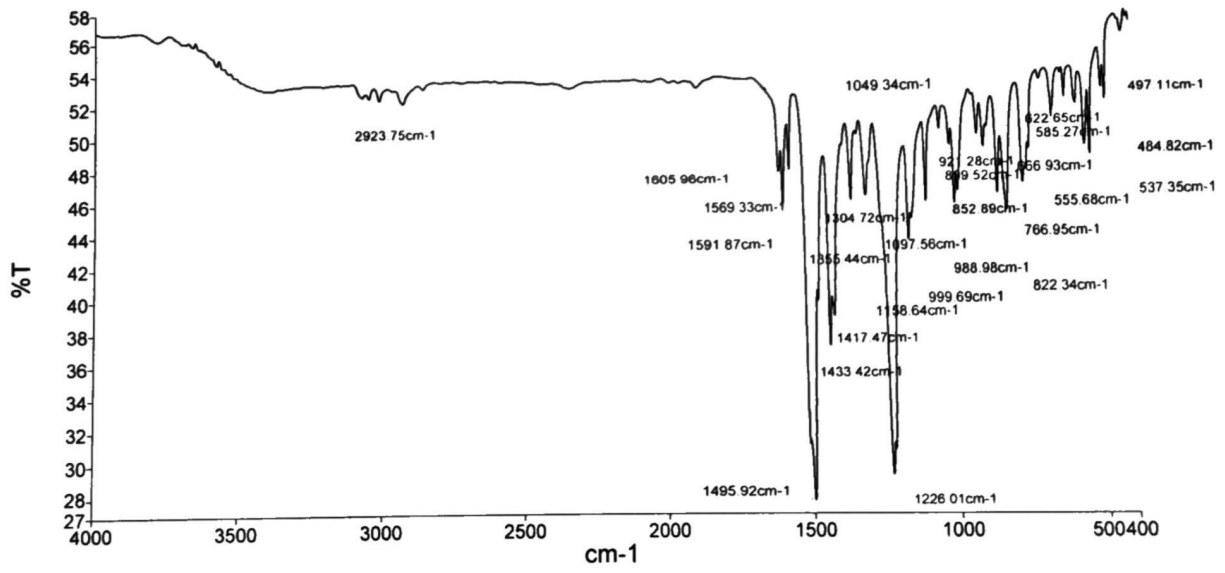

Fig. S3: FTIR spectra of complex 2.

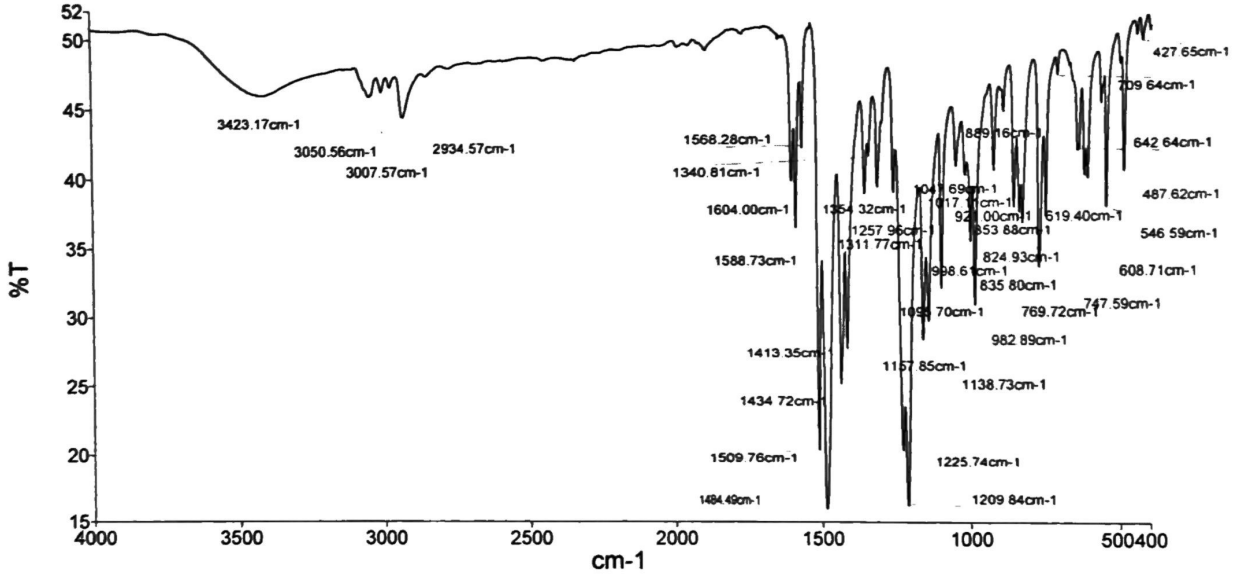

Fig. S4: FTIR spectra of complex 3.

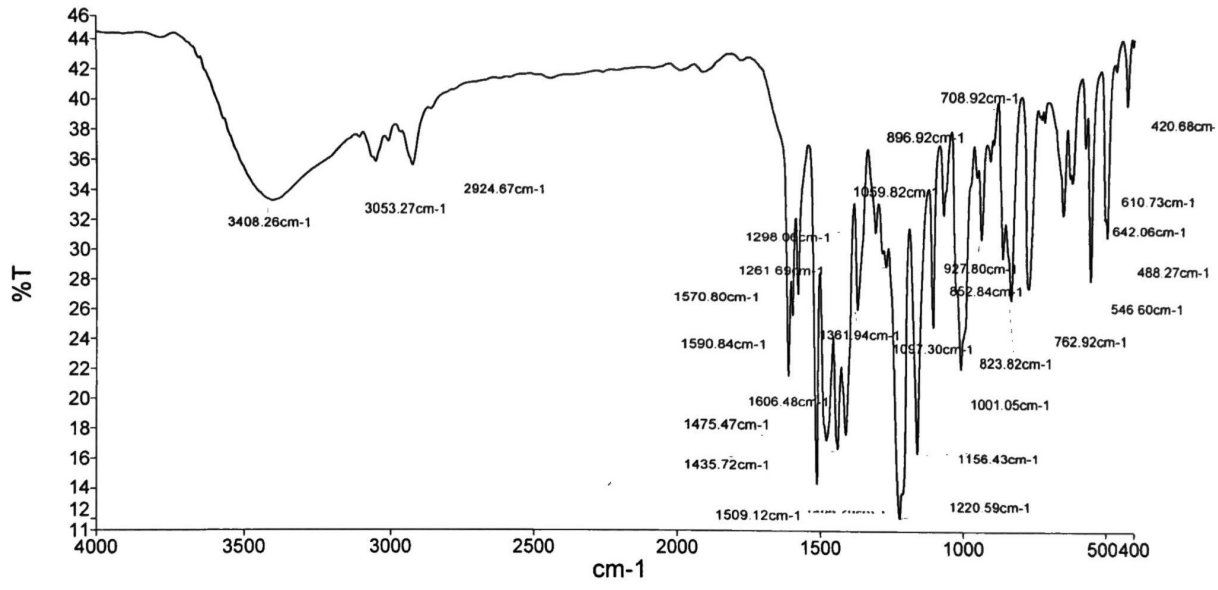

Fig. S5: FTIR spectra of complex 4.

2. NMR Spectra:

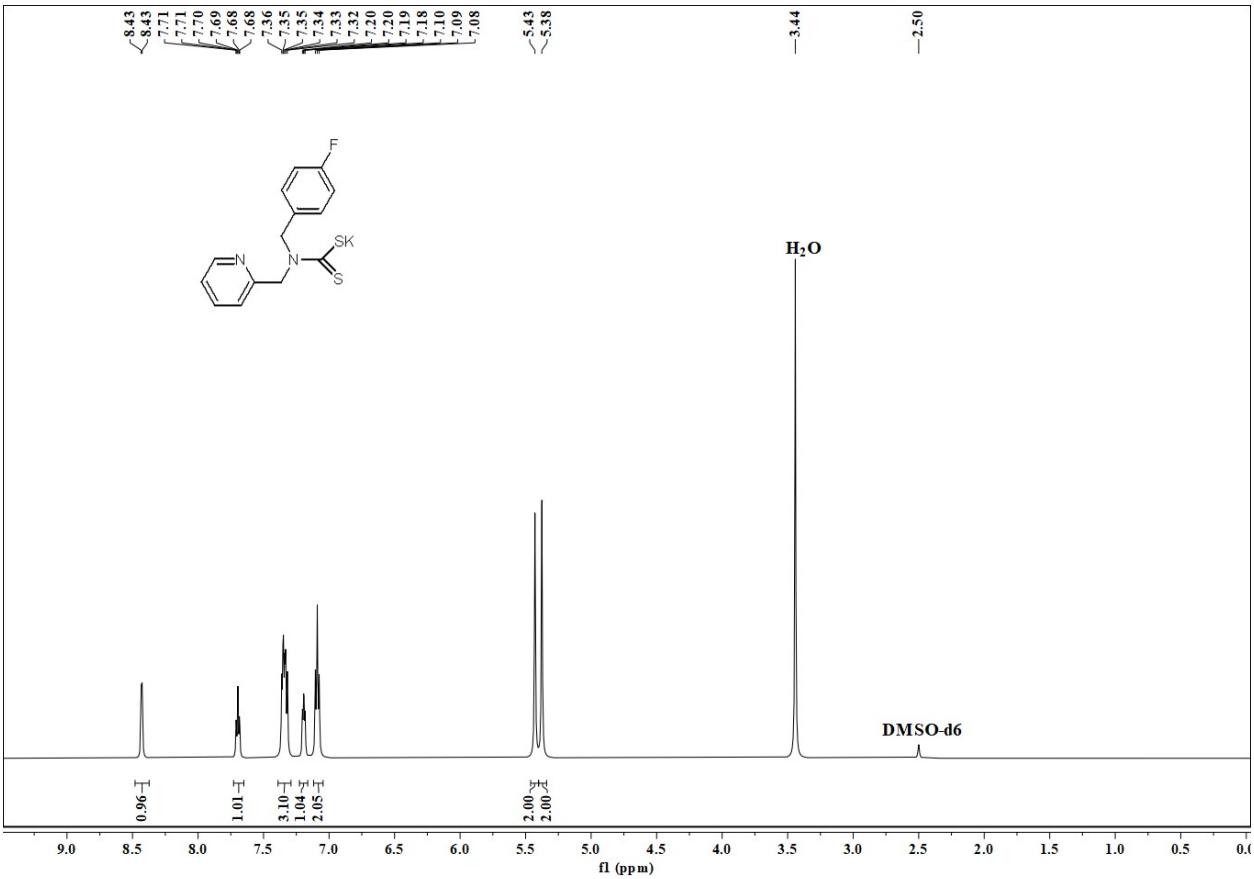

Fig. S6: ^{1}H NMR spectrum of ligand.

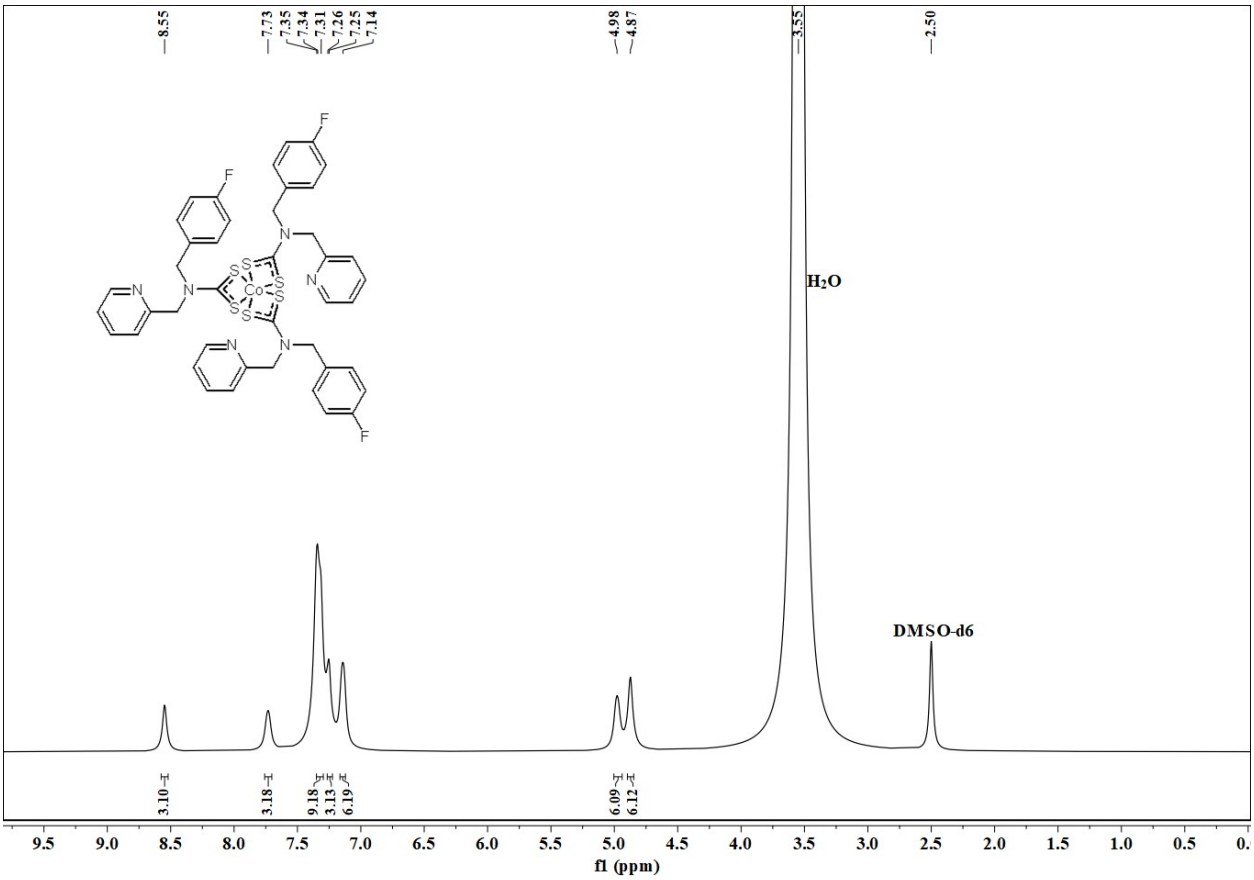

Fig. S7: ^{1}H NMR spectrum of complex **1**.

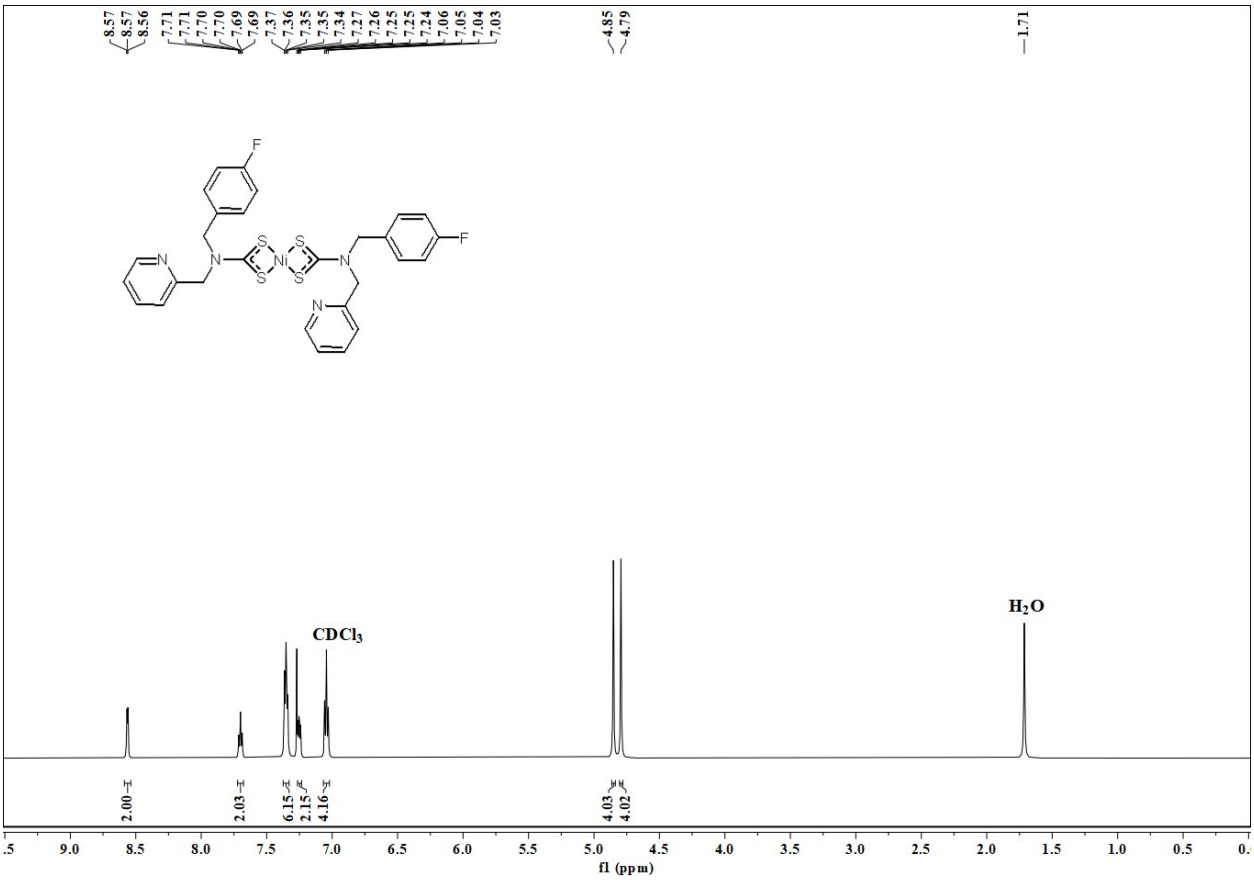

Fig. S8: ^{1}H NMR spectrum of complex **2**.

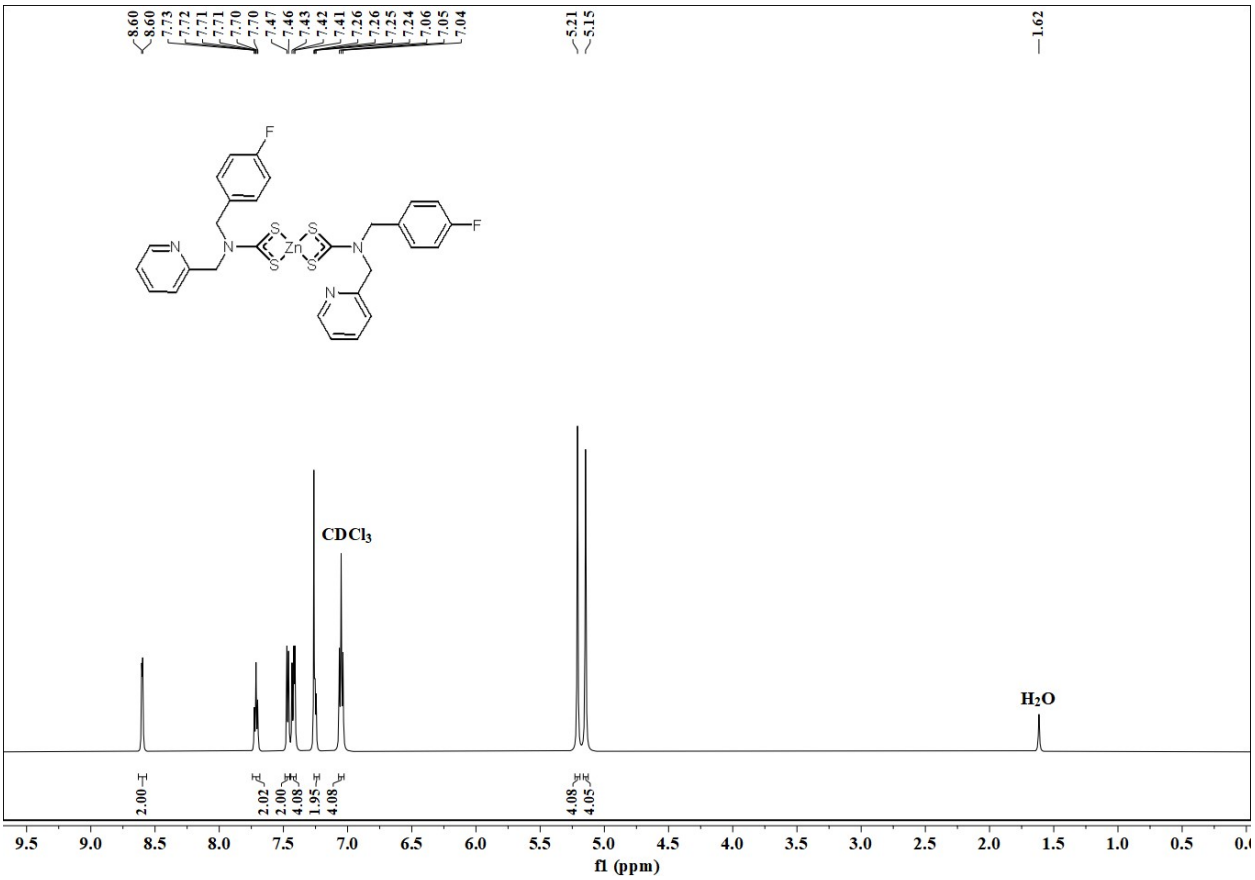

Fig. S9: ^{1}H NMR spectrum of complex **4**.

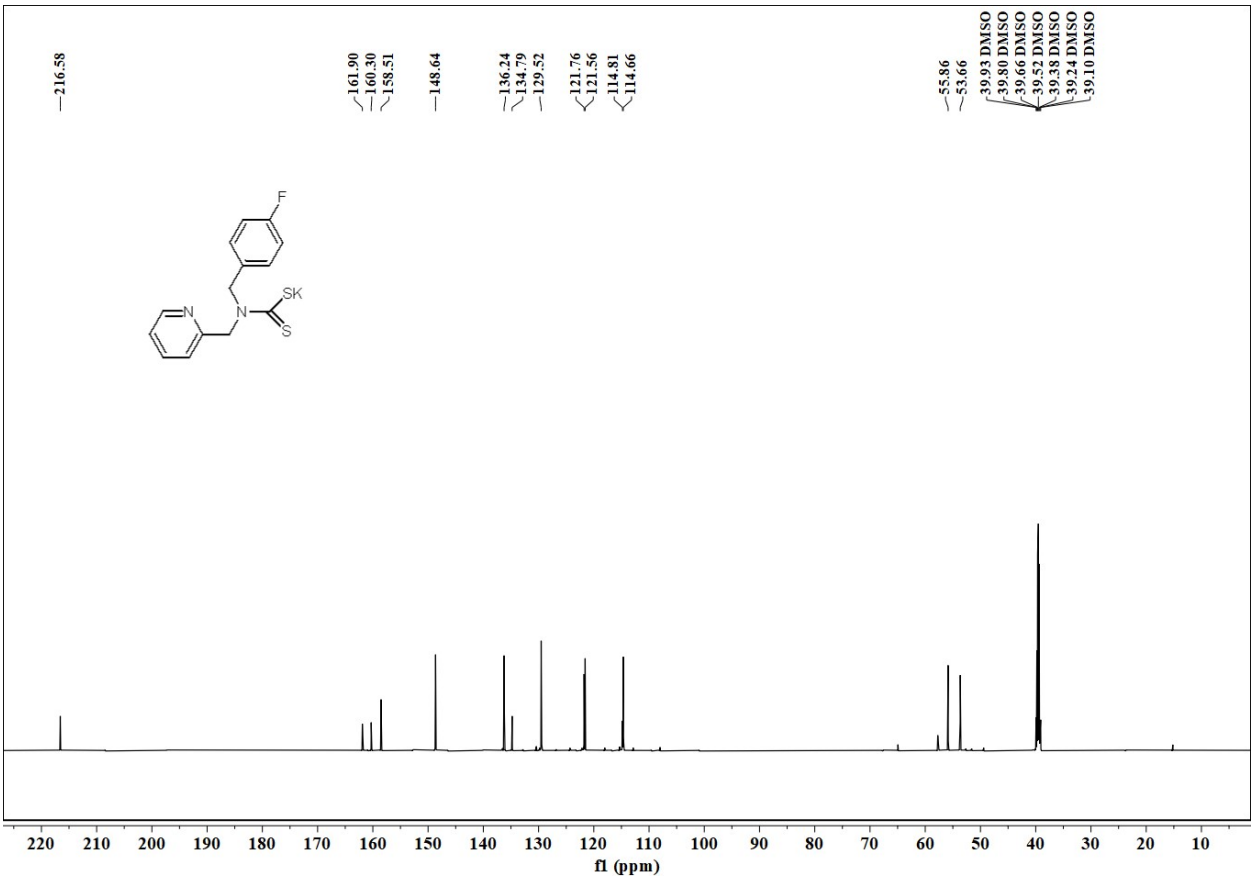

Fig. S10: ^{13}C NMR spectrum of Ligand.

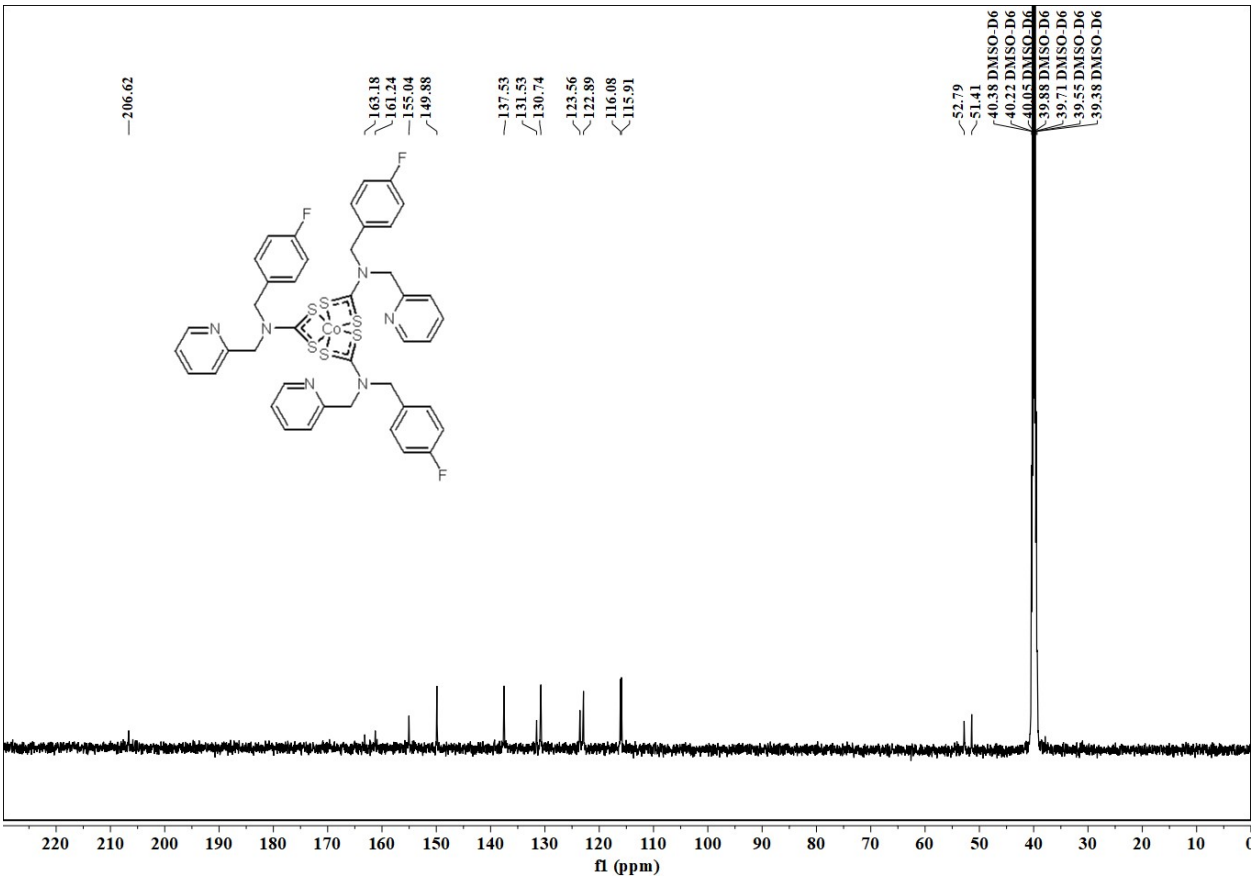

Fig. S11: ^{13}C NMR spectrum of complex **1**.

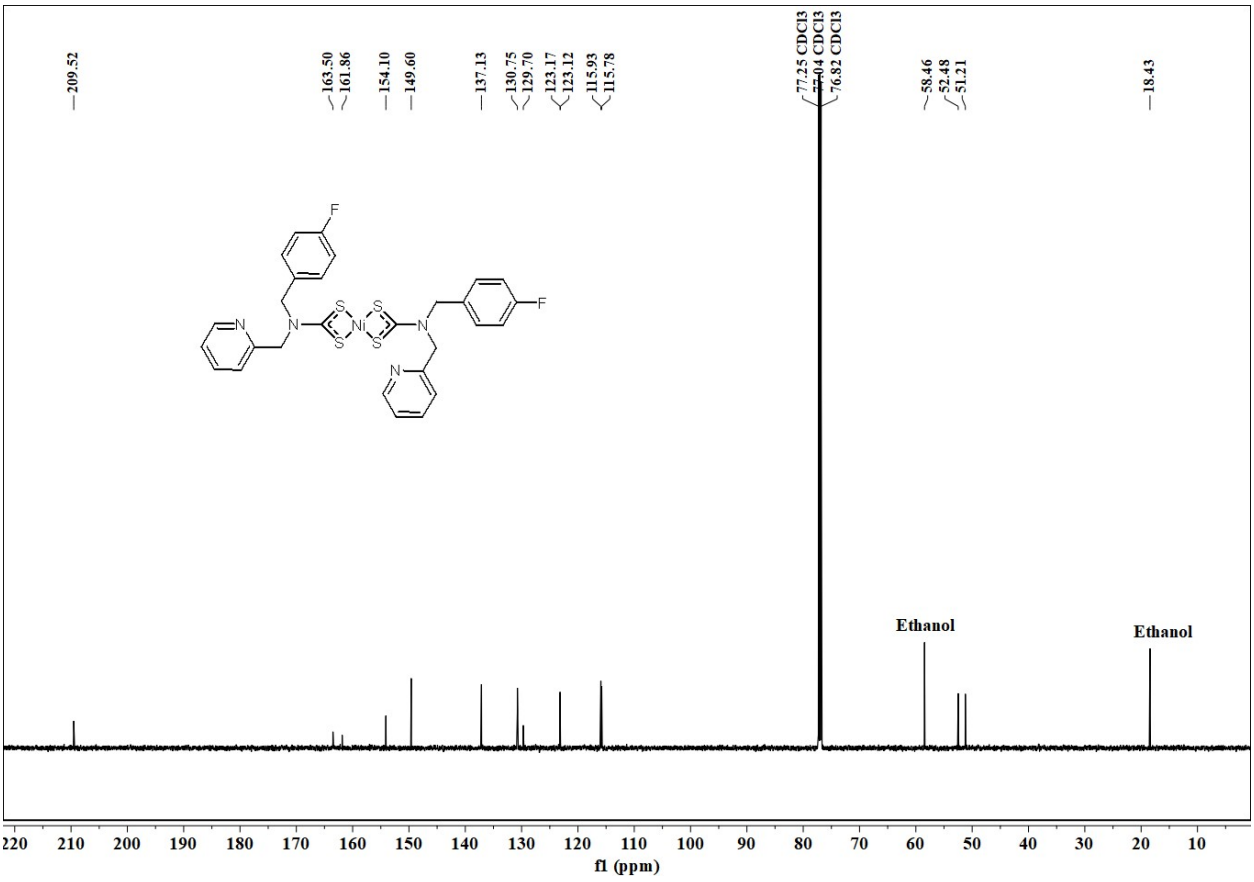

Fig. S12: ^{13}C NMR spectrum of complex **2**.

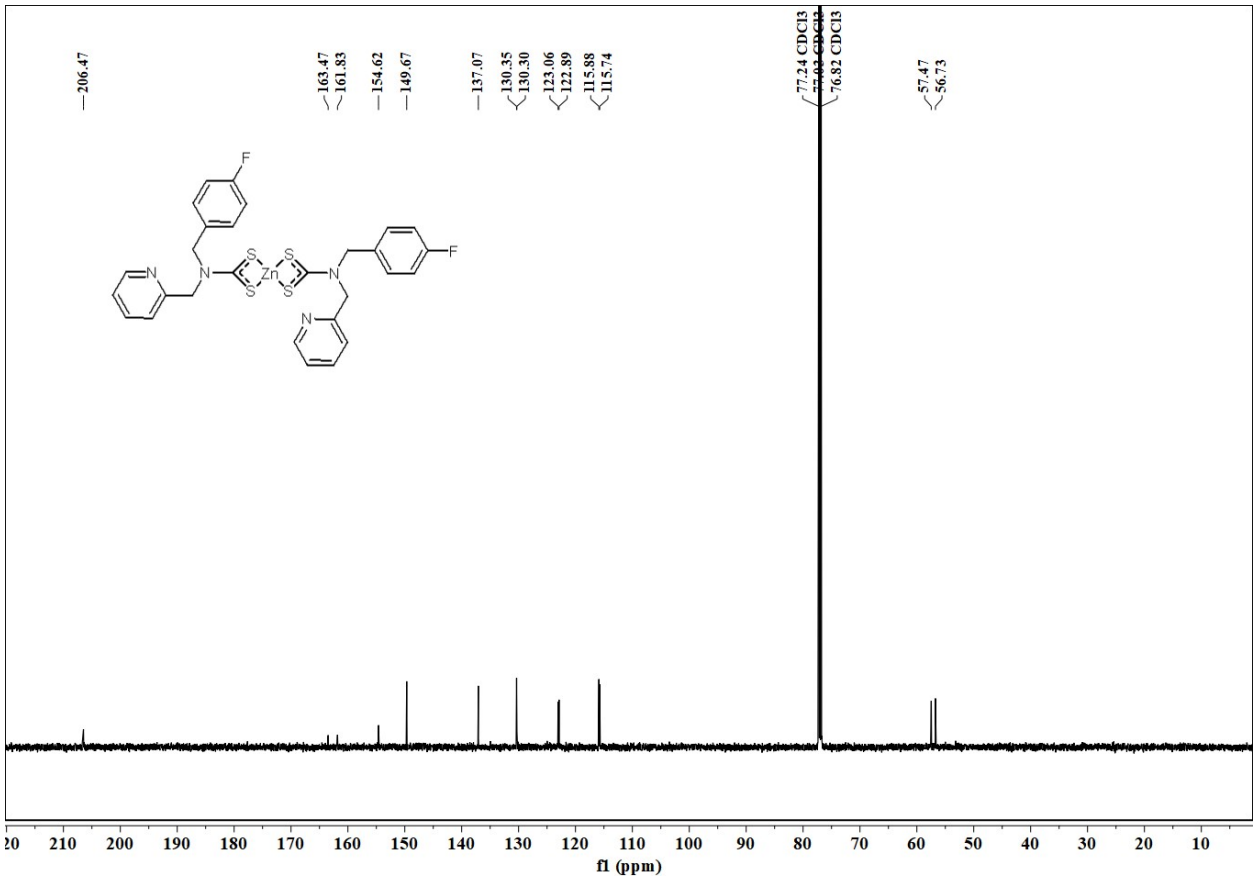

Fig. S13: ^{13}C NMR spectrum of complex **4**.

3. HRMS Spectra:

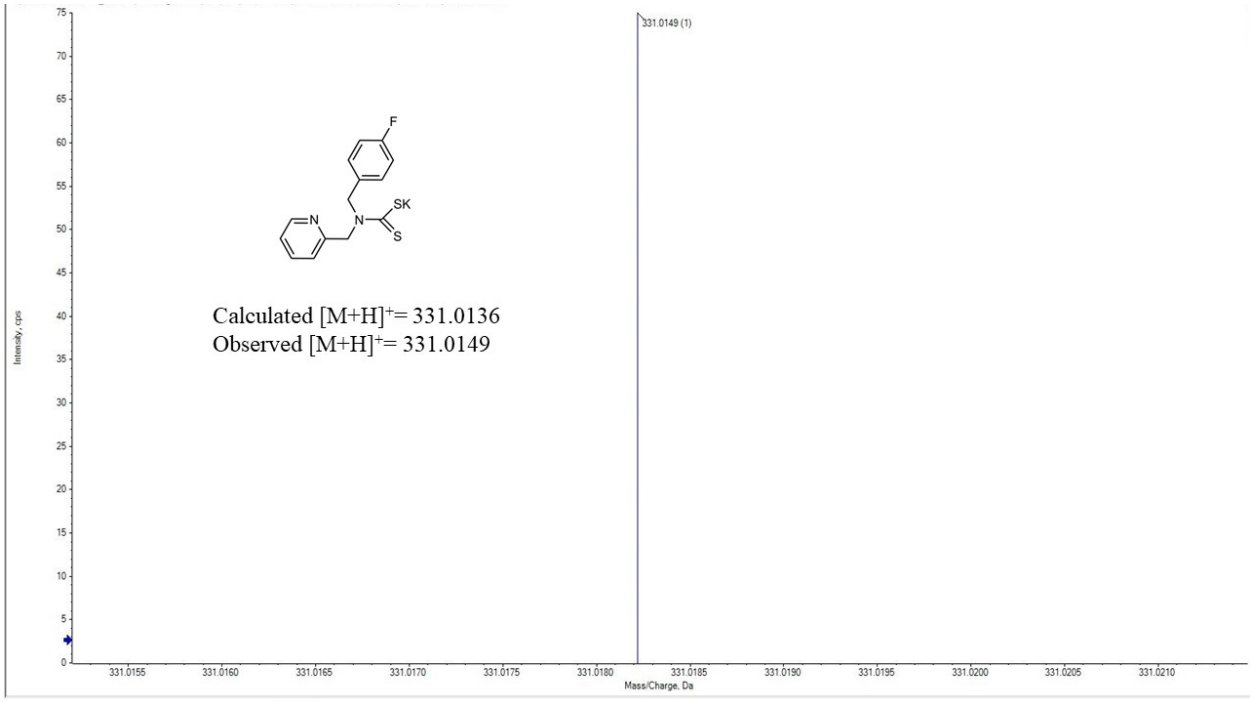

Fig. S14: HRMS spectrum of ligand.

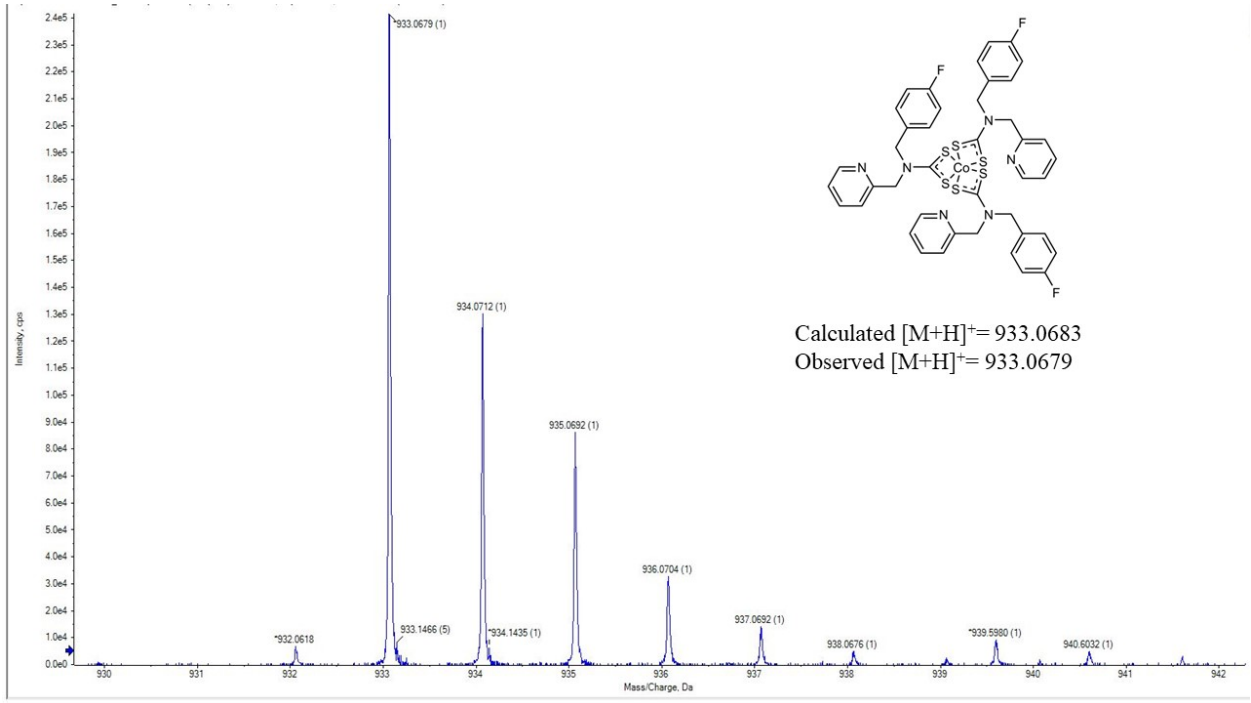

Fig. S15: HRMS spectrum of complex **1**.

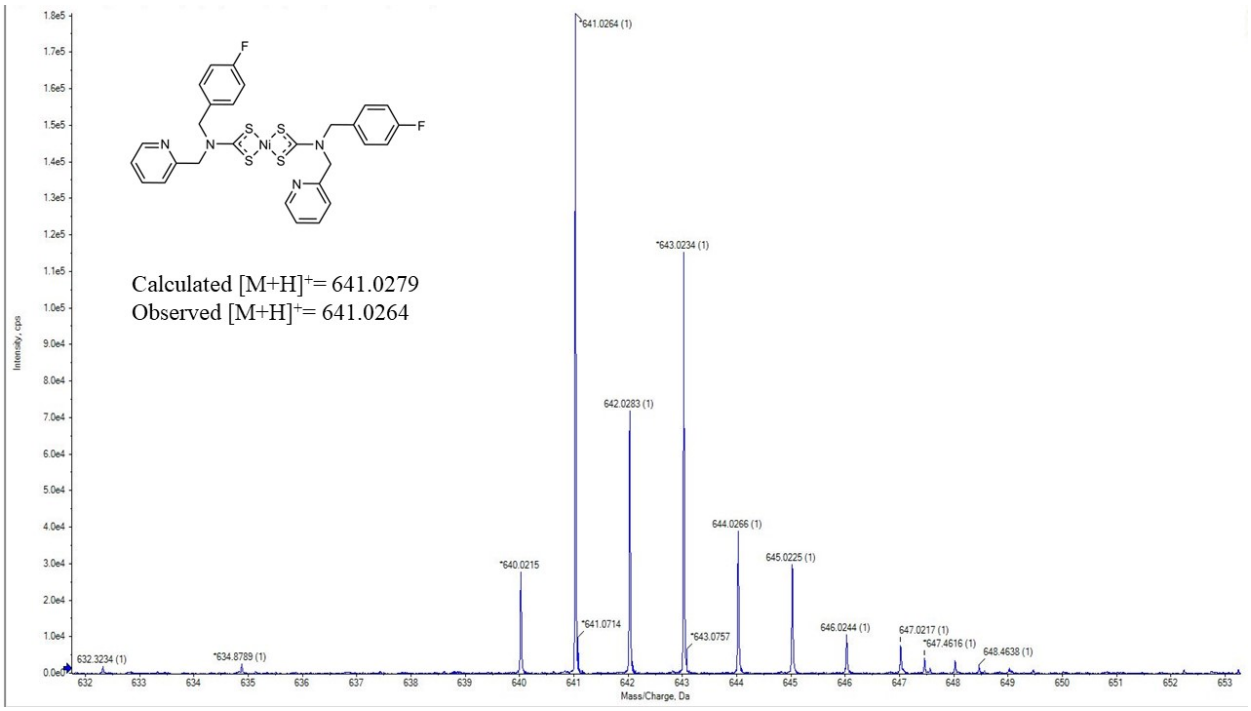

Fig. S16: HRMS spectrum of complex **2**.

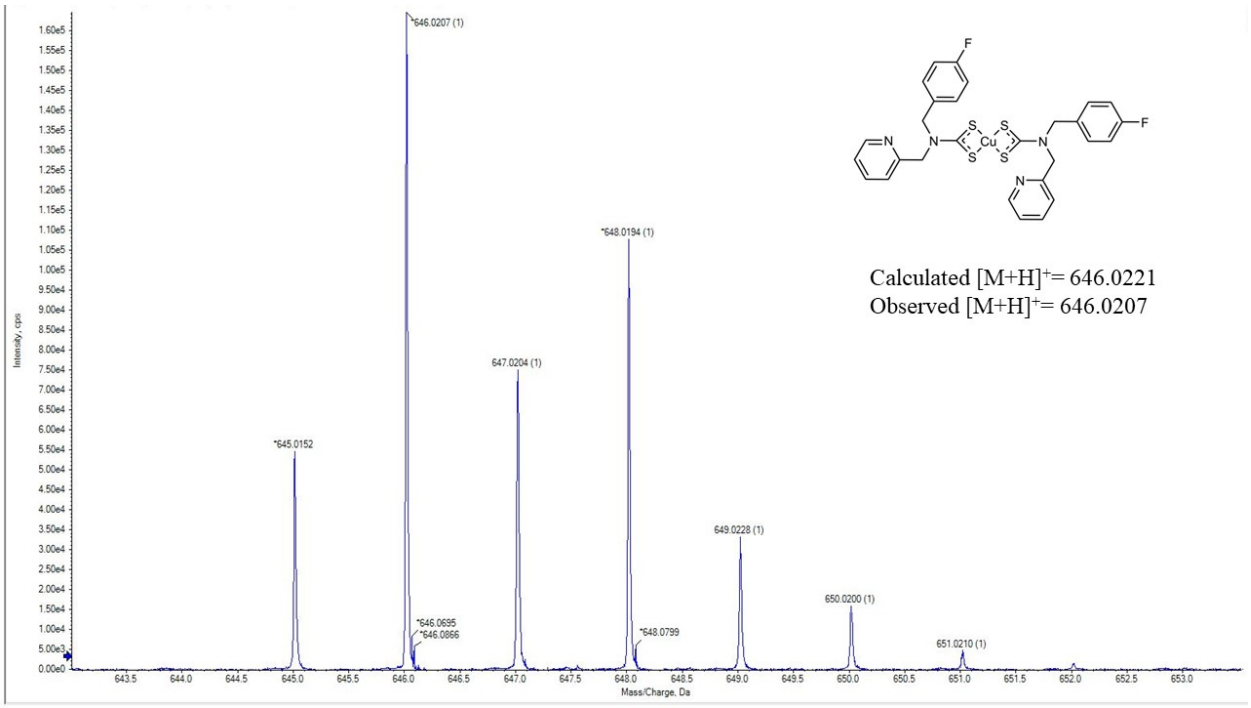

Fig. S17: HRMS spectrum of complex **3**.

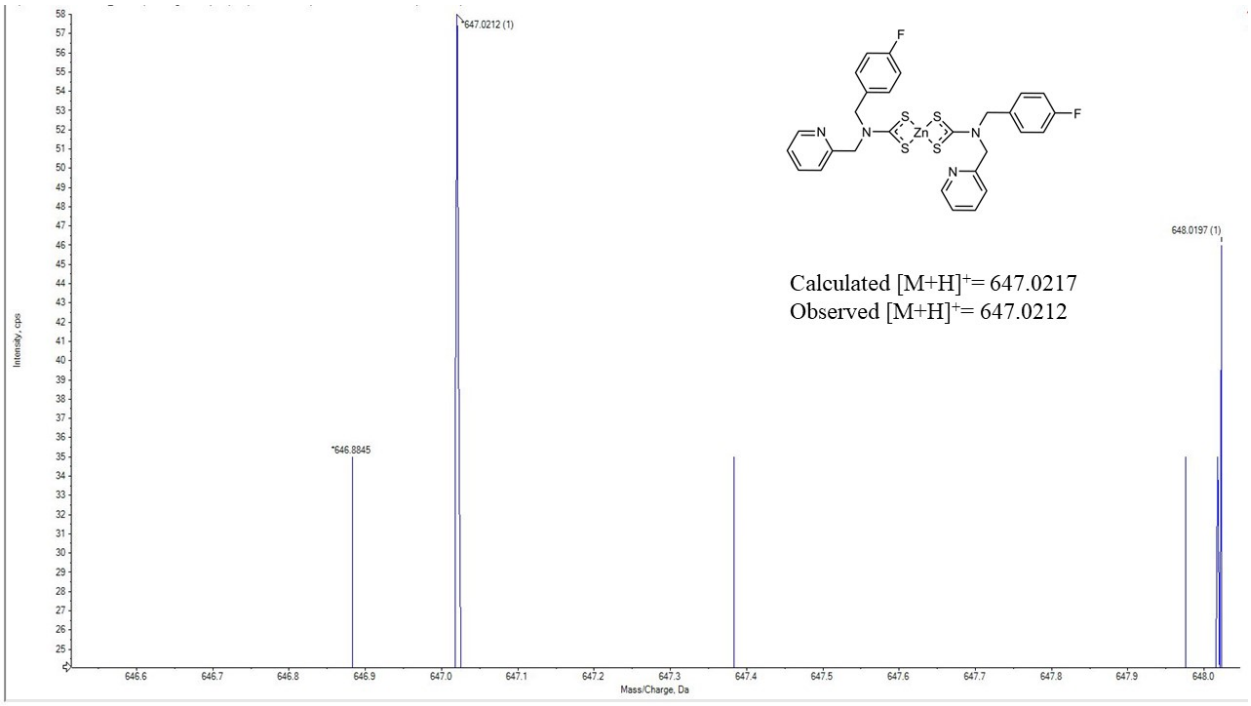

Fig. S18: HRMS spectrum of complex **4**.

4. X-ray crystallography

X-Ray diffraction measurements of complexes **1** and **2** were performed using Oxford Gemini and Bruker three-circle diffractometer equipped with a CrysAlisPro/CrysAlis CCD software using a graphite mono-chromated Mo Kα (λ= 0.71073 Å) radiation source at 296 K. The details of the temperature and monochromator of diffractometers are mentioned in the crystallographic data tables. Multi-scan absorption correction was applied to the X-ray data collection for all the compounds. The structures were solved by direct methods (SHELXS-08) and refined against all data by full matrix least-square on F^2 using anisotropic displacement parameters for all non-hydrogen atoms. All hydrogen atoms were included in the refinement at geometrically ideal position and refined with a riding model[1]. The MERCURY package and ORTEP-3 for Windows program were used for generating structures[2,3].

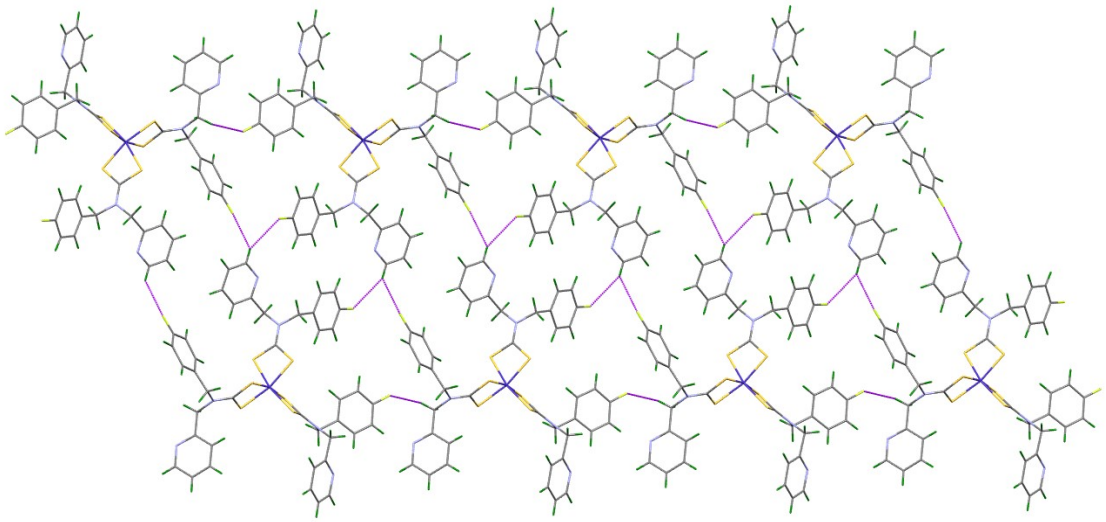

Fig. S19: Showing C-H···F hydrogen bonding interactions leading to a wave-like architecture of complex **1**.

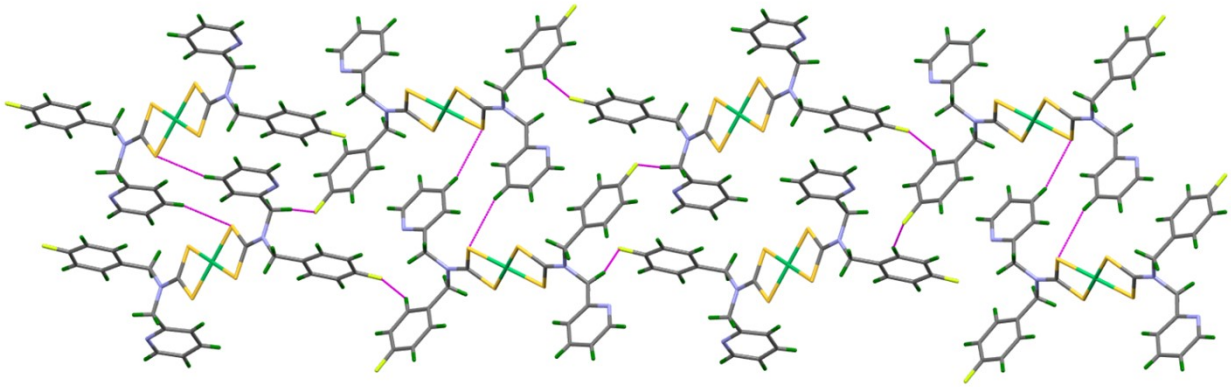

Fig. S20: Showing C-H···S and C-H···F hydrogen bonding interactions leading to supramolecular architecture of complex **2**.

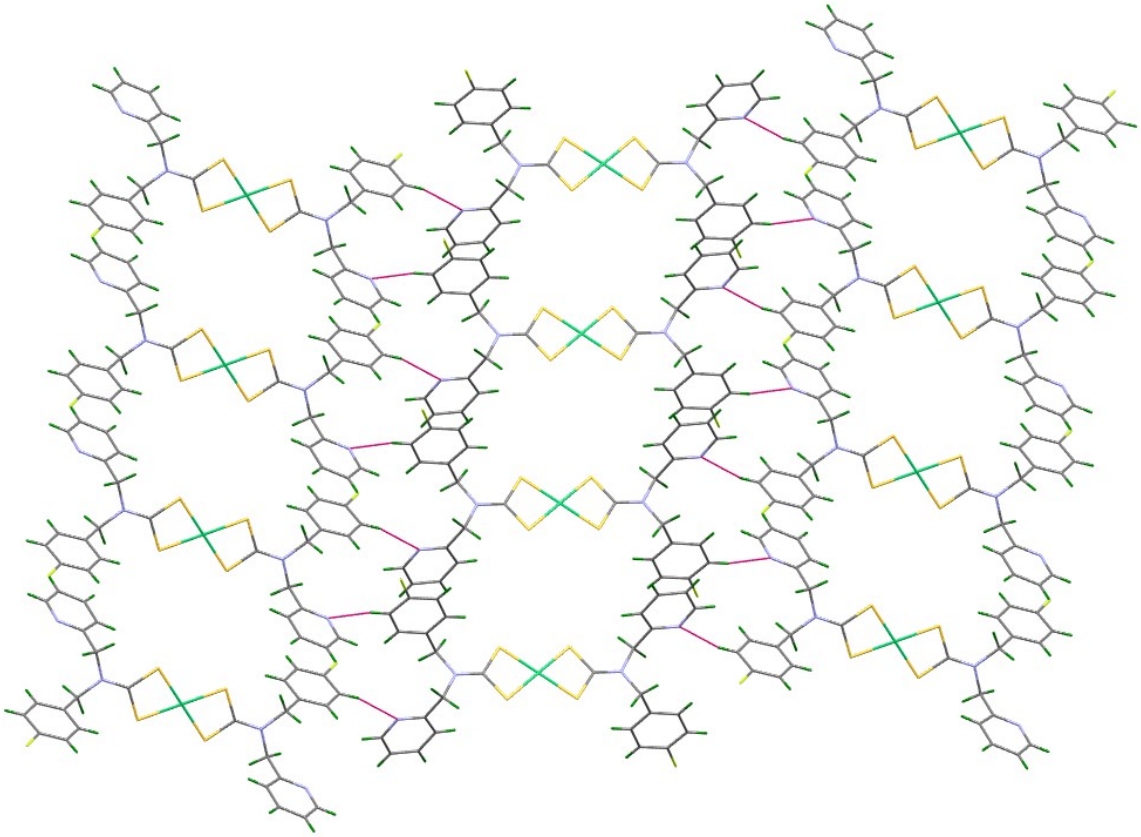

Fig. S21: Showing C-H···N hydrogen bonding interactions leading to ladder like architectures of complex **2**.

Table S1. Bond lengsth (Å) and angles (°) for complex **1**

Bond length (Å)		**Bond angle (°)**	
Co(1)-S(4)	2.2574(11)	S(4)-Co(1)-S(6)	93.92(4)
Co(1)-S(6)	2.2590(11)	S(4)-Co(1)-S(3)	76.57(4)
Co(1)-S(3)	2.2667(10)	S(6)-Co(1)-S(3)	93.78(4)
Co(1)-S(2)	2.2661(11)	S(4)-Co(1)-S(2)	167.28(4)
Co(1)-S(5)	2.2765(10)	S(6)-Co(1)-S(2)	93.87(4)
Co(1)-S(1)	2.2841(10)	S(3)-Co(1)-S(2)	92.89(4)
S(5)-C(29)	1.710(4)	S(4)-Co(1)-S(5)	91.82(4)
S(3)-C(15)	1.715(4)	S(6)-Co(1)-S(5)	76.48(4)
S(4)-C(15)	1.714(4)	S(2)-Co(1)-S(5)	99.78(4)

S(1)-C(1)	1.714(4)	S(4)-Co(1)-S(1)	96.80(4)
S(2)-C(1)	1.705(4)	S(6)-Co(1)-S(1)	167.96(5)
S(6)-C(29)	1.707(4)	S(3)-Co(1)-S(1)	94.03(4)
N(3)-C(15)	1.323(5)	S(2)-Co(1)-S(1)	76.61(4)
N(3)-C(22)	1.454(5)	S(5)-Co(1)-S(1)	97.65(4)
N(3)-C(16)	1.466(5)	S(4)-Co(1)-S(6)	93.92(4)
N(5)-C(29)	1.324(4)	S(4)-Co(1)-S(3)	76.57(4)

Table S2. Bond length (Å) and angles (°) for complex **2**

Bond length (Å)		**Bond angle (º)**	
Ni-S(1)#1	2.1976(9)	S(1)#1-Ni-S(2)	100.73(3)
Ni-S(1)	2.1977(10)	S(1)-Ni-S(2)	79.27(3)
Ni-S(2)	2.2089(9)	S(1)#1-Ni-S(2)#1	79.27(3)
Ni-S(2)#1	2.2090(9)	S(1)-Ni-S(2)#1	100.73(3)
S(2)-C(1)	1.711(4)	S(2)-Ni-S(2)#1	180.0
S(1)-C(1)	1.721(4)	C(1)-S(2)-Ni	85.31(12)
N(1)-C(1)	1.325(4)	C(1)-S(1)-Ni	85.44(12)
N(1)-C(2)	1.470(4)	C(1)-N(1)-C(2)	122.3(3)
N(1)-C(8)	1.471(4)	C(1)-N(1)-C(8)	121.7(3)
F-C(12)	1.367(5)	C(2)-N(1)-C(8)	115.9(3)
N(2)-C(7)	1.336(5)	C(7)-N(2)-C(3)	115.6(3)
N(2)-C(3)	1.346(4)	N(1)-C(2)-C(3)	113.0(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y+1,-z+1

Table S3. Hydrogen bond parameters for Complex-1.

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(16)-H(16B)...S(3)	0.97	2.60	3.090(4)	111.5
C(2)-H(2A)...F(3)#1	0.97	2.53	3.409(7)	151.0
C(22)-H(22B)...S(4)	0.97	2.57	3.076(4)	112.8

C(36)-H(36A)...S(6)	0.97	2.55	3.073(4)	113.5
C(36)-H(36B)...N(6)	0.97	2.69	3.342(6)	124.8
C(21)-H(21)...F(12A^a)#2	0.93	2.62	3.363(11)	137.6

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

Table S4. Hydrogen bond parameters for Complex-2.

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
C(2)-H(2A)...S(1)	0.97	2.57	3.085(4)	113.3
C(2)-H(2B)...F#2	0.97	2.58	3.122(5)	115.2
C(8)-H(8A)...S(2)	0.97	2.59	3.102(4)	113.3
C(13)-H(13)...N(2)#3	0.93	2.66	3.519(5)	153.4
C(6)-H(6)...S(2)#4	0.93	3.02	3.903(5)	160.0
C(2)-H(2A)...S(1)	0.97	2.57	3.085(4)	113.3
C(2)-H(2B)...F#2	0.97	2.58	3.122(5)	115.2
C(8)-H(8A)...S(2)	0.97	2.59	3.102(4)	113.3
C(13)-H(13)...N(2)#3	0.93	2.66	3.519(5)	153.4
C(6)-H(6)...S(2)#4	0.93	3.02	3.903(5)	160.0

Symmetry transformations used to generate equivalent atoms:

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

5. Biological application

Fig. S22: Animals showing catalepsy during experiments induced via clonidine and haloperidol.

Table S5: Effect of various synthetic compounds on clonidine induced catalepsy.

Time (Min.)	Control	Induced Control	fbpm	1	2	3	4	Chlorpheniramine maleate
30	3.3±0.78	103.75±7.47	110.75±5.35	107.75±6.08	98.25±6.25	78.75±10.80	118.75±8.34	42.25±5.97
60	3.26±1.09	108.75±6.88	117.5±9.63	102±8.39	102.25±7.37	69.25±6.57	123.75±8.96	54.75±7.47

90	3.87±1.14	105.5±5.92	104.25±2.52	115.25±6.60	119.5±9.42	65.5±9.53	129.75±7.52	80.75±5.02
120	2.87±1.1	120.25±9.04	92.25±6.47	92±6.62	91.5±8.14	60.5±6.53	108.75±8.98	62.5±6.07
150	2.85±1.08	74.75±5.17	85.75±6.57	86.25±9.62	84±5.40	51±5.67	98.5±8.17	40.25±6.81
180	2.6±0.69	60.25±6.92	83.5±7.81	96.5±6.70	79.75±6.16	45.75±5.48	84±5.70	29.5±3.22

Values are expressed as mean±SEM, two-way ANOVA followed by Dunnette's test, p value <0.01 considered as significant, (n=6).

Table S6: Effect of various synthetic compounds on haloperidol induced catalepsy.

Time (Min.)	**Control**	**Induced Control**	**fbpm**	**1**	**2**	**3**	**4**	**Chlorpheniramine maleate**
30	3.35±1.04	67.75±17.75	91.5±5.90	109.75±7.02	107.25±8.03	93.75±7.58	156±14.60	54.75±12.57
60	3.43±1.10	134.25±27.46	86.25±7.26	104.5±9.40	114.75±10.41	131±7.42	181.75±17.26	67.25±12.61
90	4.6±0.68	142±30.36	106.25±6.28	119.5±6.40	134.5±4.34	120.25±10.13	123.75±18.08	98.25±9.36
120	2.37±0.70	129.25±19.77	113±12.90	94.25±7.40	120.25±5.20	109±9.60	173.75±29.68	77.25±9.48
150	3.35±0.89	149.5±18.90	102±6.12	88.75±9.23	110.75±8.18	121±9.63	118.5±28.73	70.25±5.86
180	3.07±0.94	176±37.50	92.5±6.03	99±6.60	104±8.89	93.25±20.62	77±9.56	62±4.91

Values are expressed as mean±SEM, two-way ANOVA followed by Dunnette's test, p value <0.01 considered as significant, (n=6).

6. References:

[1] G.M. Sheldrick, ActaCrystallogr. Section A, 2008, 64, 112-122.

[2] C.F. Macrae, I.J. Bruno, J.A. Chisholm, P.R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J.Van de Streek, P.A., Wood, Appl. Cryst., 2008, 41, 466-470.

[3] L.J. Farrugia, J. Appl. Cryst., 2012, 45, 849-854.