Electronic Supplementary Information (ESI)

Identification of potent anticancer copper(II) complexes containing tripodal bis[2-ethyl-di(3,5-dialkyl-1*H*-pyrazol-1-yl)]amine moiety†

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X-ray crystal structure analysis

The X-ray single-crystal data of compounds were collected on a Bruker-AXS APEX-II CCD diffractometer at 100(2) K. The crystallographic data, conditions retained for the intensity data collection and some features of the structure refinements are listed in Table S1. The intensities were collected with Mo-Kα radiation (λ= 0.71073 Å). Data processing, Lorentz-polarization and absorption corrections were performed using SAINT, APEX and the SADABS computer programs.[S1] The structures were solved by direct methods and refined by full-matrix least-squares methods on F^2, using the SHELX program package.[S2] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were located from difference Fourier maps, assigned with isotropic displacement factors and included in the final refinement cycles by use of geometrical constraints. Further programs used: Mercury [S3],[S3] Olex[S4] and Platon.[S5]

References

S1. (a) Bruker (2005) SAINT v. 7.23; Bruker (2006) APEX 2, v. 2.0-2, Bruker AXS Inc., Madison, Wisconsin, USA, 2005.;
(b) G. M. Sheldrick, SADABS v. 2, University of Goettingen, Germany, 2001.

S2. (a) G. M. Sheldrick, *Acta Cryst.* 2008, **A64**, 112-122.
(b) G. M. Sheldrick, *Acta Cryst.* 2015, **C71**, 3-8.

S3. C. F. Macrae, P. R. Edington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, T. Towler and J. van de Streek, *J. Appl. Cryst.* 2009, **39**, 453;

S4. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann *J. Appl. Cryst.* 2009, **42**, 339-341.

S5. A. L. Speck, "PLATON , a multipurpose crystallographic tool." Utrecht University, Utrecht, The Netherlands, 2001.

Table S1. Crystallographic data and processing parameters

Compound	**1-ClO_4**	**2-ClO_4**	**4-ClO_4**	**5-PF_6**
Empirical formula	$C_{21.5}H_{32}Cl_2CuN_6O_{4.5}$	$C_{22}H_{32}Cl_2CuN_6O_6$	$C_{20}H_{31}Cl_2CuN_7O_4$	$C_{25}H_{33}ClCuF_6N_7P$
Formula mass	580.98	610.97	567.96	675.54
System	Triclinic	Monoclinic	Monoclinic	Triclinic
Space group	P-1	C 2/c	C 2/c	P-1
a (Å)	10.9839(4)	20.3521(9)	21.6070(7)	10.5750(6)
b (Å)	12.3595(5)	20.4978(9)	12.1524(4)	12.4521(7)
c (Å)	12.5141(5)	15.1917(7)	19.2083(6)	13.0589(8)
α (°)	115.690(2)	90	90	69.599(3)
β (°)	108.072(2)	104.876(2)	102.879(2)	68.263(3)
γ (°)	100.254(2)	90	90	71.979(3)
V ($Å^3$)	1355.13(10)	6125.2(5)	4916.9(3)	1464.70(15)
Z	2	8	8	2
T (K)	100(2)	100(2)	100(2)	100(2)
μ (mm^{-1})	1.043	0.930	1.147	0.959
D_{calc} (Mg/m^3)	1.424	1.325	1.534	1.532
θ max (°)	26.999	25.999	30.050	27.000
Data collected	26771	79236	153829	51180
Unique refl. / R_{int}	5889 / 0.0770	6021 / 0.0346	7171 / 0.0230	6401 / 0.0414
Parameters / Restraints	526 / 269	368 / 18	379 /42	375 / 0
Goodness-of-Fit on F^2	1.136	1.073	1.057	1.036
R1 / wR2 (all data)	0.0544 / 0.1509	0.0515 / 0.1386	0.0308 / 0.0741	0.0373 / 0.0875

Table S2. Selected bond distances (Å) and bond angles (°) of complexes **1-ClO$_4$**, **2-ClO$_4$**, **4-ClO$_4$** and **5-PF$_6$.**

1-ClO$_4$			
Cu1-N2A	2.11(2)	Cu1-N6	2.231(3)
Cu1-N1	2.098(3)	Cu1-Cl1	2.2762(10)
Cu1-N4A	2.146(17)		
N2A-Cu1-N4A	163.0(9)	N1-Cu1-Cl1	147.71(11)
2-ClO$_4$			
Cu1-N4	1.997(3)	Cu1-N2	1.995(3)
Cu1-N6	2.246(3)	Cu1-Cl1	2.3023(11)
Cu1-N1	2.134(2)		
N2-Cu1-N4	166.34(12)	N1-Cu1-Cl1	153.33(8)
4-ClO$_4$			
Cu1-N1	2.2248(13)	Cu1-N7	2.053(15)
Cu1-N3	2.0199(13)	Cu1-N9	2.213(12)
Cu1-N5	1.9880(12)	Cu1-Cl1	2.2727(5)
N3-Cu1-N5	165.67(5)	N1-Cu1-Cl1	142.10(4)
5-PF$_6$			
Cu1-N5	2.0027(18)	Cu1-N1	2.1710(18)
Cu1-N7	2.0164(18)	Cu1-Cl1	2.2810(6)
Cu1-N3	2.1551(19)		
N5-Cu1-N7	165.72(7)	N1-Cu1-Cl1	148.25(5)
6 [Cu(bedmpzp)Cl]PF$_6$ [a)]			
Cu1-N1	2.005(4)	Cu1-N3	1.991(4)
Cu1-N2	2.147(4)	Cl1-N1	2.2868(12)
Cu1-N5	2.291(4)		
N2-Cu1-Cl1	161.64(11)	N3-Cu1-N1	166.17(15)

[a)] Data taken from Ref 38

Table S3. Non-covalent interactions of **1-ClO_4**

5-Membered Ring (1) N3A --> N4A --> C12A --> C11A --> C10A
5-Membered Ring (2) N5 --> N6 --> C19 --> C18 --> C17
5-Membered Ring (3) N3B --> N4B --> C10B --> C11B --> C12B
6-Membered Ring (4) N2A --> C2A --> C3A --> C4A --> C5A --> C6A
6-Membered Ring (5) N2B --> C2B --> C3B --> C4B --> C5B --> C6B

Ring-Interactions with Cg-Cg Distances < 6.0 Ang., Alpha < 20.000 Deg., Beta < 60.0 Deg.

- Cg(I) = Plane number I (= ring number in () above)
- Alpha = Dihedral Angle between Planes I and J (Deg)
- Beta = Angle Cg(I)-->Cg(J) or Cg(I)-->Me vector and normal to plane I (Deg)
- Gamma = Angle Cg(I)-->Cg(J) vector and normal to plane J (Deg)
- Cg-Cg = Distance between ring Centroids (Ang.)
- CgI_Perp = Perpendicular distance of Cg(I) on ring J (Ang.)
- CgJ_Perp = Perpendicular distance of Cg(J) on ring I (Ang.)
- Slippage = Distance between Cg(I) and Perpendicular Projection of Cg(J) on Ring I (Ang).

Cg(I)	Cg(J)	[ARU(J)]	Cg-Cg	Alpha	Beta	Gamma	CgI_Perp	CgJ_Perp	Slippage
Cg1	Cg1	[2667.01]	4.980(8)	0	49.8	49.8	3.214(7)	3.214(7)	3.805
Cg1	Cg2	[1555.01]	4.967(6)	88.0(7)	57.0	50.5	3.160(5)	2.707(2)	
Cg1	Cg3	[2666.01]	4.809(15)	12	37.1	38.0	3.790(7)	3.835(14)	2.901
Cg1	Cg4	[2666.01]	4.577(9)	20.5(9)	33.4	28.2	4.035(6)	3.821(7)	
Cg1	Cg5	[2667.01]	5.262(10)	12	50.9	41.8	3.922(6)	3.317(9)	4.085
Cg2	Cg1	[1555.01]	4.967(6)	88.0(7)	50.5	57.0	2.707(2)	3.160(5)	
Cg2	Cg1	[2667.01]	4.932(5)	88.0(7)	10.9	84.1	0.508(2)	4.843(5)	
Cg2	Cg2	[2556.01]	4.620(3)	0.0(2)	41.5	41.5	3.4577(14)	3.4577(14)	3.064
Cg2	Cg3	[1555.01]	5.029(12)	80	50.9	59.4	2.563(2)	3.170(11)	
Cg2	Cg4	[1555.01]	5.357(6)	73.6(6)	50.8	62.9	2.445(2)	3.383(5)	
Cg2	Cg5	[1555.01]	5.304(9)	77.8(8)	51.6	62.2	2.477(2)	3.291(7)	
Cg2	Cg5	[2667.01]	4.890(7)	77.8(8)	15.5	71.4	1.562(2)	4.712(7)	
Cg3	Cg1	[2666.01]	4.809(15)	12	38.0	37.1	3.835(14)	3.790(7)	2.961
Cg3	Cg2	[1555.01]	5.028(12)	80	59.4	50.9	3.170(11)	2.563(2)	
Cg3	Cg5	[2666.01]	4.517(16)	23	36.0	28.9	3.953(14)	3.655(9)	
Cg4	Cg1	[2666.01]	4.576(9)	20.5(9)	28.2	33.4	3.821(7)	4.034(6)	
Cg4	Cg3	[2555.01]	5.685(12)	10	58.0	60.4	2.806(7)	3.015(14)	4.820
Cg4	Cg4	[2555.01]	5.386(8)	0.0(9)	55.9	55.9	3.021(7)	3.021(7)	4.459
Cg4	Cg5	[2666.01]	4.295(11)	29	26.6	26.1	3.857(7)	3.840(9)	
Cg5	Cg1	[2667.01]	5.262(10)	12	41.8	50.9	3.317(9)	3.922(6)	3.508
Cg5	Cg3	[2666.01]	4.517(16)	23	28.9	36.0	3.656(9)	3.953(14)	
Cg5	Cg4	[2666.01]	4.295(11)	29	26.1	26.6	3.840(9)	3.857(7)	
Cg5	Cg5	[2667.01]	5.558(12)	0	43.4	43.4	4.039(9)	4.039(9)	3.817

[2667] = 1-X,1-Y,2-Z
[1555] = X,Y,Z
[2666] = 1-X,1-Y,1-Z
[2556] = -X,-Y,1-Z
[2555] = -X,-Y,-Z

Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma < 40.0 Deg)

- Cg(J) = Center of gravity of ring J (Plane number above)
- H-Perp = Perpendicular distance of H to ring plane J
- Gamma = Angle between Cg-H vector and ring J normal
- X-H..Cg = X-H-Cg angle (degrees)
- X..Cg = Distance of X to Cg (Angstrom)

X--H(I)	Res(I)	Cg(J)	[ARU(J)]	H..Cg	H-Perp	Gamma	X-H..Cg	X..Cg
C11A	-H11A	Cg2	[2667.01]	2.90	2.87	8.74	155	3.787(10)
C20	-H20A	Cg2	[2556.01]	2.71	-2.70	3.15	142	3.535(4)
C13B	-H13F	Cg5	[2666.01]	2.93	2.30	38.43	144	3.774(16)

[2667] = 1-X,1-Y,2-Z
[2556] = -X,-Y,1-Z
[2666] = 1-X,1-Y,1-Z

The Cg(I) refer to the Ring Centre-of-Gravity numbers given in () in the Ring-Analysis above

Cg(I)	x	y	z	Xo	Yo	Zo
Cg1	0.5951(5)	0.5379(5)	0.8574(5)	2.024(6)	1.213(7)	8.698(5)
Cg2	0.12824(16)	0.21432(16)	0.66024(13)	-1.6260(19)	-1.497(2)	6.6976(14)
Cg3	0.1297(10)	0.2385(10)	0.2697(10)	-0.147(12)	1.224(14)	2.736(10)
Cg4	0.1427(6)	0.2187(5)	0.2381(5)	0.162(6)	1.180(7)	2.415(5)
Cg5	0.6322(7)	0.5448(7)	0.8583(7)	2.414(9)	1.291(9)	8.707(7)

Analysis of Potential Hydrogen Bonds and Schemes

Res	Donor---	H....Acceptor	[ARU]	D-H	H...A	D...A	D-H...A
4>O5	--H90	..	?	0.91			
1>C8A	--H8AB	..O1	[1555.02]	0.99	2.57	3.512(9)	158
1>C8A	--H8AB	..O3	[1555.02]	0.99	2.41	2.936(8)	112'
1>C4A	--H4A	..O2	[1454.02]	0.95	2.53	3.267(9)	135
1>C7A	--H7A3	..Cl1	[]	0.98	2.63	3.42(2)	137
1>C5A	--H5A	..O4	[1454.02]	0.95	2.51	3.363(17)	149
1>C1A	--H1AA	..Cl1	[2666.01]	0.99	2.73	3.711(8)	174
1>C9A	--H9AB	..Cl1	[2666.01]	0.99	2.80	3.593(8)	138
1>C14A	--H14A	..Cl1	[]	0.98	2.60	3.415(17)	141
C18	--H18	..O3	[1455.02]	0.95	2.38	3.263(7)	155

:: No Classic Hydrogen Bonds Found

Translation of ARU-Code to CIF and Equivalent Position Code

[2666.] = [2_666] = 1-x,1-y,1-z
[1454.] = [1_454] = -1+x,y,-1+z
[1455.] = [1_455] = -1+x,y,z

Table S4. Non-covalent interactions of **2-ClO$_4$**

5-Membered Ring (1) Cu1 --> N1 --> C1 --> C2 --> N2
5-Membered Ring (2) N3 --> N4 --> C13 --> C12 --> C11
5-Membered Ring (3) N5 --> N6 --> C20 --> C19 --> C18
6-Membered Ring (4) Cu1 --> N1 --> C9 --> C10 --> N3 --> N4
6-Membered Ring (6) N2 --> C2 --> C3 --> C4 --> C5 --> C6

Ring-Interactions with Cg-Cg Distances < 6.0 Ang., Alpha < 20.000 Deg., Beta < 60.0 Deg.

- Cg(I) = Plane number I (= ring number in () above)
- Alpha = Dihedral Angle between Planes I and J (Deg)
- Beta = Angle Cg(I)-->Cg(J) or Cg(I)-->Me vector and normal to plane I (Deg)
- Gamma = Angle Cg(I)-->Cg(J) vector and normal to plane J (Deg)
- Cg-Cg = Distance between ring Centroids (Ang.)
- CgI_Perp = Perpendicular distance of Cg(I) on ring J (Ang.)
- CgJ_Perp = Perpendicular distance of Cg(J) on ring I (Ang.)
- Slippage = Distance between Cg(I) and Perpendicular Projection of Cg(J) on Ring I (Ang).

Cg(I)	Cg(J)	[ARU(J)]	Cg-Cg	Alpha	Beta	Gamma	CgI_Perp	CgJ_Perp	Slippage
Cg2	Cg6	[7667.01]	4.576(2)	23.12(19)	13.2	26.1	4.1092(15)	4.4553(14)	
Cg3	Cg3	[7666.01]	4.519(2)	0.0(2)	43.7	43.7	3.2677(17)	3.2677(17)	3.122
Cg3	Cg6	[1555.01]	4.868(2)	84.6(2)	35.1	51.9	3.0034(16)	3.9813(15)	
Cg6	Cg2	[7667.01]	4.576(2)	23.12(19)	26.1	13.2	4.4552(14)	4.1092(15)	
Cg6	Cg3	[1555.01]	4.868(2)	84.6(2)	51.9	35.1	3.9812(15)	3.0034(16)	
Cg6	Cg6	[2656.01]	4.343(2)	6.16(17)	39.3	39.3	3.3611(14)	3.3610(14)	2.750

[7667] = 3/2-X,3/2-Y,2-Z
[7666] = 3/2-X,3/2-Y,1-Z
[1555] = X,Y,Z
[2656] = 1-X,Y,3/2-Z

Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma < 40.0 Deg)

- Cg(J) = Center of gravity of ring J (Plane number above)
- H-Perp = Perpendicular distance of H to ring plane J
- Gamma = Angle between Cg-H vector and ring J normal
- X-H..Cg = X-H-Cg angle (degrees)
- X..Cg = Distance of X to Cg (Angstrom)

X--	H(I)	Cg(J)	[ARU(J)]	H..Cg	H-Perp	Gamma	X-H..Cg	X..Cg
C8	-H8C	Cg3	[2656.01]	2.83	-2.58	24.37	148	3.704(5)
C21	-H21C	Cg3	[7666.01]	2.61	2.61	1.25	139	3.417(5)

[2656] = 1-X,Y,3/2-Z
[7666] = 3/2-X,3/2-Y,1-Z

The Cg(I) refer to the Ring Centre-of-Gravity numbers given in () in the Ring-Analysis above

Cg(I)	x	y	z	Xo	Yo	Zo
Cg2	0.89122(8)	0.66376(8)	0.85354(10)	14.8094(17)	13.6057(17)	12.5321(15)
Cg3	0.71782(8)	0.80202(8)	0.61328(11)	12.2172(17)	16.4397(17)	9.0045(16)
Cg6	0.59747(7)	0.78234(7)	0.85063(10)	8.8423(15)	16.0362(14)	12.4895(14)

Analysis of Potential Hydrogen Bonds and Schemes

Res	Donor---	H....Acceptor	[ARU]	D-H	H...A	D...A	D-H...A
C1	--H1A	..Cl1	[7667.01]	0.99	2.69	3.453(4)	134
C5	--H5	..O7B	[6656.02]	0.95	2.41	3.309(9)	157
C6	--H6	..O5	[6656.02]	0.95	2.59	3.322(5)	134
C10	--H10B	..O6B	[4565.02]	0.99	2.51	3.257(9)	132
C14	--H14A	..O5	[1555.02]	0.98	2.44	3.339(6)	153
C14	--H14B	..O7A	[4565.02]	0.98	2.22	3.163(10)	160
C14	--H14C	..O7B	[2756.02]	0.98	2.30	3.187(12)	150
C15	--H15C	..Cl1	[]	0.98	2.79	3.512(4)	131
C16	--H16A	..O1	[2656.01]	0.99	2.59	3.377(5)	136
C17	--H17A	..O4	[1555.02]	0.99	2.60	3.545(6)	160

C19	--H19	..O6A	[7666.02]	0.95	2.56	3.456(11)	156
C19	--H19	..O6B	[7666.02]	0.95	2.55	3.498(9)	172'
C21	--H21A	..O4	[7666.02]	0.98	2.55	3.474(5)	157
C22	--H22B	..Cl1	[]	0.98	2.72	3.652(4)	159
C22	--H22C	..O5	[6656.02]	0.98	2.48	3.372(6)	151

:: No Classic Hydrogen Bonds Found

Translation of ARU-Code to CIF and Equivalent Position Code

[7667.] = [7_667] = 3/2-x,3/2-y,2-z
[2656.] = [2_656] = 1-x,y,3/2-z
[6656.] = [4_656] = 3/2-x,1/2+y,3/2-z
[4565.] = [6_566] = x,1-y,1/2+z
[2756.] = [2_756] = 2-x,y,3/2-z
[7666.] = [7_666] = 3/2-x,3/2-y,1-z

Table S5. Non-covalent interactions of **4-ClO_4**

5-Membered Ring (1) N2 --> N3 --> C4 --> C3 --> C2
5-Membered Ring (2) N4 --> N5 --> C11 --> C10 --> C9
5-Membered Ring (3) N8 --> N9 --> C1C --> C1B --> C1A
5-Membered Ring (4) N6 --> N7 --> C18 --> C17 --> C16

Ring-Interactions with Cg-Cg Distances <6.0 Ang., Alpha <20.0 Deg., Beta <60.0 Deg.

- Cg(I) = Plane number I (= ring number in () above)
- Alpha = Dihedral Angle between Planes I and J (Deg)
- Beta = Angle Cg(I)-->Cg(J) or Cg(I)-->Me vector and normal to plane I (Deg)
- Gamma = Angle Cg(I)-->Cg(J) vector and normal to plane J (Deg)
- Cg-Cg = Distance between ring Centroids (Ang.)
- CgI_Perp = Perpendicular distance of Cg(I) on ring J (Ang.)
- CgJ_Perp = Perpendicular distance of Cg(J) on ring I (Ang.)
- Slippage = Distance between Cg(I) and Perpendicular Projection of Cg(J) on Ring I (Ang).

Cg(I)	Cg(J)	[ARU(J)]	Cg-Cg	Alpha	Beta	Gamma	CgI_Perp	CgJ_Perp	Slippage
Cg1	Cg1	[7636.01]	5.6364(9)	0.00(9)	44.4	44.4	4.0252(7)	4.0251(7)	3.946
Cg1	Cg2	[7636.01]	5.5172(10)	44.99(10)	24.5	56.4	3.0551(7)	5.0185(7)	
Cg1	Cg3	[1555.01]	4.525(5)	73.8(5)	29.1	44.7	3.2185(6)	3.953(5)	
Cg1	Cg3	[2756.01]	5.596(5)	76.0(5)	26.0	82.8	0.7006(6)	5.029(5)	
Cg1	Cg4	[1555.01]	4.366(5)	66.6(5)	31.1	36.2	3.5227(6)	3.737(5)	
Cg1	Cg4	[2756.01]	5.473(6)	76.5(5)	28.3	85.2	0.4586(6)	4.819(5)	
Cg2	Cg1	[7636.01]	5.5171(10)	44.99(10)	56.4	24.5	5.0186(7)	3.0550(7)	
Cg2	Cg3	[6646.01]	5.547(5)	85.2(5)	12.3	74.2	1.5062(7)	5.419(5)	
Cg2	Cg4	[6646.01]	5.919(5)	79.9(5)	11.9	69.1	2.1090(7)	5.792(5)	
Cg3	Cg1	[1555.01]	4.526(5)	73.8(5)	44.7	29.1	3.953(5)	3.2186(6)	
Cg3	Cg2	[1555.01]	4.994(5)	89.0(5)	57.4	68.9	1.796(5)	2.6912(7)	
Cg3	Cg3	[2756.01]	4.602(8)	3.9(7)	34.6	34.6	3.788(5)	3.787(5)	2.615
Cg3	Cg4	[2756.01]	4.609(8)	11.2(7)	34.7	41.0	3.477(5)	3.789(5)	2.624
Cg4	Cg1	[1555.01]	4.366(5)	66.6(5)	36.2	31.1	3.737(5)	3.5228(6)	
Cg4	Cg3	[2756.01]	4.608(8)	11.2(7)	41.0	34.7	3.789(5)	3.476(5)	3.025
Cg4	Cg4	[2756.01]	4.583(8)	16.9(8)	39.8	39.8	3.522(5)	3.522(5)	2.933

[7636] = 3/2-X,-3/2-Y,1-Z
[1555] = X,Y,Z
[2756] = 2-X,Y,3/2-Z
[6646] = 3/2-X,-1/2+Y,3/2-Z

Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma < 40.0 Deg)

- Cg(J) = Center of gravity of ring J (Plane number above)
- H-Perp = Perpendicular distance of H to ring plane J
- Gamma = Angle between Cg-H vector and ring J normal
- X-H..Cg = X-H-Cg angle (degrees)
- X..Cg = Distance of X to Cg (Angstrom)

X	--H(I)	Cg(J)	[ARU(J)]	H..Cg	H-Perp	Gamma	X-H..Cg	X..Cg
C1D	-H1DC	Cg2	[6656.01]	2.78	-2.67	16.13	130	3.485(9)
C8	-H8B	Cg1	[7636.01]	2.89	-2.81	13.30	145	3.7393(16)

[6656] = 3/2-X,1/2+Y,3/2-Z
[7636] = 3/2-X,-3/2-Y,1-Z

The Cg(I) refer to the Ring Centre-of-Gravity numbers given in () in the Ring-Analysis above

Cg(I)	x	y	z	Xo	Yo	Zo
Cg1	0.87880(3)	-0.69603(6)	0.55256(3)	16.6230(7)	-8.4584(7)	10.3468(6)
Cg2	0.66406(3)	-0.59649(6)	0.70930(4)	11.3120(7)	-7.2487(7)	13.2817(7)
Cg3	0.8986(2)	-0.5359(4)	0.7691(3)	16.123(5)	-6.513(5)	14.402(5)
Cg4	0.8989(3)	-0.5674(4)	0.7687(3)	16.132(6)	-6.896(5)	14.394(5)

Analysis of Potential Hydrogen Bonds and Schemes

Res	Donor---	H....Acceptor	[ARU]	D-H	H...A	D...A	D-H...A
C3	--H3	..O3	[2756.02]	0.95	2.60	3.547(2)	176
1>C1D	--H1DB	..O2	[3747.02]	0.98	2.37	3.326(7)	165
C5	--H5B	..O2	[2756.02]	0.98	2.59	3.517(2)	158
C5	--H5C	..O2	[4544.02]	0.98	2.58	3.512(2)	159
C6	--H6A	..Cl1	[]	0.98	2.71	3.5781(18)	148
C8	--H8A	..O3	[6656.02]	0.99	2.58	3.307(2)	130
C14	--H14B	..N2	[]	0.99	2.56	2.954(2)	104

:: No Classic Hydrogen Bonds Found

Translation of ARU-Code to CIF and Equivalent Position Code

[3747.] = [5_747] = 2-x,-1-y,2-z
[6656.] = [4_656] = 3/2-x,1/2+y,3/2-z
[4544.] = [6_545] = x,-1-y,-1/2+z
[2756.] = [2_756] = 2-x,y,3/2-z

Table S6. Non-covalent interactions of **5-PF_6**

5-Membered Ring (1) Cu1 --> N1 --> C15 --> N6 --> N7
5-Membered Ring (2) N2 --> N3 --> C5 --> C4 --> C3
5-Membered Ring (3) N4 --> N5 --> C12 --> C11 --> C10
5-Membered Ring (4) N6 --> N7 --> C18 --> C17 --> C16
6-Membered Ring (5) Cu1 --> N1 --> C1 --> C2 --> N2
6-Membered Ring (6) Cu1 --> N1 --> C8 --> C9 --> N4 --> N5
6-Membered Ring (7) C19 --> C20 --> C21 --> C22 --> C23 --> C24

Ring-Interactions with Cg-Cg Distances < 6.0 Ang., Alpha < 20.000 Deg. and Beta < 60.0 Deg.

- Cg(I) = Plane number I (= ring number in () above)
- Alpha = Dihedral Angle between Planes I and J (Deg)
- Beta = Angle Cg(I)-->Cg(J) or Cg(I)-->Me vector and normal to plane I (Deg)
- Gamma = Angle Cg(I)-->Cg(J) vector and normal to plane J (Deg)
- Cg-Cg = Distance between ring Centroids (Ang.)
- CgI_Perp = Perpendicular distance of Cg(I) on ring J (Ang.)
- CgJ_Perp = Perpendicular distance of Cg(J) on ring I (Ang.)
- Slippage = Distance between Cg(I) and Perpendicular Projection of Cg(J) on Ring I (Ang).
- P,Q,R,S = J-Plane Parameters for Carth. Coord. (Xo, Yo, Zo)

Cg(I)	Cg(J)	[ARU(J)]	Cg-Cg	Alpha	Beta	Gamma	CgI_Perp	CgJ_Perp	Slippage
Cg2	Cg3	[1555.01]	4.8080(16)	81.61(14)	49.6	56.2	2.6745(10)	3.1158(10)	
Cg2	Cg3	[2666.01]	4.8080(16)	81.61(14)	14.9	84.0	0.5372(10)	4.9575(10)	
Cg2	Cg4	[1555.01]	4.9143(15)	82.00(14)	51.5	51.6	3.0498(10)	3.0613(10)	
Cg3	Cg2	[1555.01]	4.8079(16)	81.61(14)	56.2	49.6	3.1157(10)	2.6744(10)	
Cg3	Cg3	[2666.01]	4.7155(16)	0.00(14)	47.1	47.1	3.2116(10)	3.2117(10)	3.453
Cg3	Cg4	[2656.01]	4.6885(15)	14.96(13)	38.6	24.3	4.2747(10)	3.6666(9)	2.922
Cg3	Cg7	[2656.01]	4.5953(14)	36.31(13)	21.4	54.0	2.6996(10)	4.2779(10)	
Cg4	Cg2	[1555.01]	4.9143(15)	82.00(14)	51.6	51.5	3.0613(10)	3.0497(10)	
Cg4	Cg3	[2656.01]	4.6885(15)	14.96(13)	24.3	38.6	3.6666(9)	4.2747(10)	1.926
Cg7	Cg2	[1545.01]	5.9825(15)	66.05(13)	8.4	62.9	2.7265(10)	5.9190(10)	
Cg7	Cg3	[2656.01]	4.5952(14)	36.31(13)	54.0	21.4	4.2778(10)	2.6995(10)	
Cg7	Cg7	[2655.01]	3.9188(16)	0.00(12)	23.2	23.2	3.6030(10)	3.6030(10)	1.541

[1555] = X,Y,Z
[2666] = 1-X,1-Y,1-Z
[2656] = 1-X,-Y,1-Z
[1545] = X,-1+Y,Z
[2655] = 1-X,-Y,-Z

Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma < 40.0 Deg)

- Cg(J) = Center of gravity of ring J (Plane number above)
- H-Perp = Perpendicular distance of H to ring plane J
- Gamma = Angle between Cg-H vector and ring J normal
- X-H..Cg = X-H-Cg angle (degrees)
- X..Cg = Distance of X to Cg (Angstrom)
- X-H, Pi = Angle of the X-H bond with the Pi-plane (i.e.' Perp. = 90 degr., Para. = 0 degr.)

X	--H(I)	Cg(J)	[ARU(J)]	H..Cg	H-Perp	Gamma	X-H..Cg	X..Cg
C6	-H6AB	Cg7	[1565.01]	2.99	-2.84	18.42	136	3.757(3)

[1565] = X,1+Y,Z

The Cg(I) refer to the Ring Centre-of-Gravity numbers given in () in the Ring-Analysis above

Cg(I)	x	y	z	Xo	Yo	Zo
Cg2	0.85610(11)	0.36457(8)	0.23978(8)	11.6173(13)	5.0875(10)	2.8046(10)
Cg3	0.43669(12)	0.31845(8)	0.55100(8)	8.5095(13)	5.5416(10)	6.4449(10)
Cg4	0.80260(9)	-0.01270(8)	0.23738(8)	9.5866(10)	0.6125(10)	2.7766(9)
Cg7	0.63537(12)	-0.12368(8)	0.06824(8)	6.5726(13)	-1.2453(10)	0.7982(9)

Potential Hydrogen Bonds and Schemes

Res	Donor---	H.Acceptor	[ARU]	D-H	H...A	D...A	D-H.A
C1	--H1AB	..N6	[]	0.99	2.60	2.986(3)	103
C1	--H1AB	..F4	[2665.02]	0.99	2.54	3.111(3)	116'
C2	--H2AB	..F2	[1555.02]	0.99	2.52	3.021(4)	111
C4	--H4	..F1	[1655.02]	0.95	2.54	3.394(4)	149
C7	--H7AB	..Cl1	[]	0.98	2.79	3.743(3)	163
C8	--H8AB	..F1	[1555.02]	0.99	2.48	3.270(3)	136
C14	--H14C	..F2	[2666.02]	0.98	2.41	3.365(3)	165
C15	--H15A	..Cl1	[2656.01]	0.99	2.57	3.491(2)	155
C25	--H25B	..Cl1	[]	0.98	2.82	3.603(2)	138

:: No Classic Hydrogen Bonds Found

Translation of ARU-Code to CIF and Equivalent Position Code
[2656.] = [2_656] = 1-x,-y,1-z
[2665.] = [2_665] = 1-x,1-y,-z
[2666.] = [2_666] = 1-x,1-y,1-z
[1655.] = [1_655] = 1+x,y,z

Table S7. Cell cycle distribution (% cells) in the individual cell cycle phases, determined by flow cytometry with the Annexin V-FITC/PI staining of the A2780 cells treated for 24 h by the equitoxic concentrations of complexes **1-PF_6**, **2-ClO_4** and **4-PF_6**. Control is represented by untreated cells. *Cisplatin* was involved for comparative purposes.

	Concentration [μM]	G0/G1 phase [average %]	SD	S phase [average %]	SD	G2/M [average %]	SD
Control		56.4	0.4	24.2	0.4	19.5	0.7
1-PF_6	3	47.3	1.0	21.3	0.8	31.4	1.7
2-$ClO_4 \cdot H_2O$	3	45.3	0.8	25.8	0.7	28.9	0.3
4-PF_6	50	31.4	1.8	26. 8	1.4	41.9	0.9
Cisplatin	30	52.4	2.8	32.8	1.7	14.8	1.2

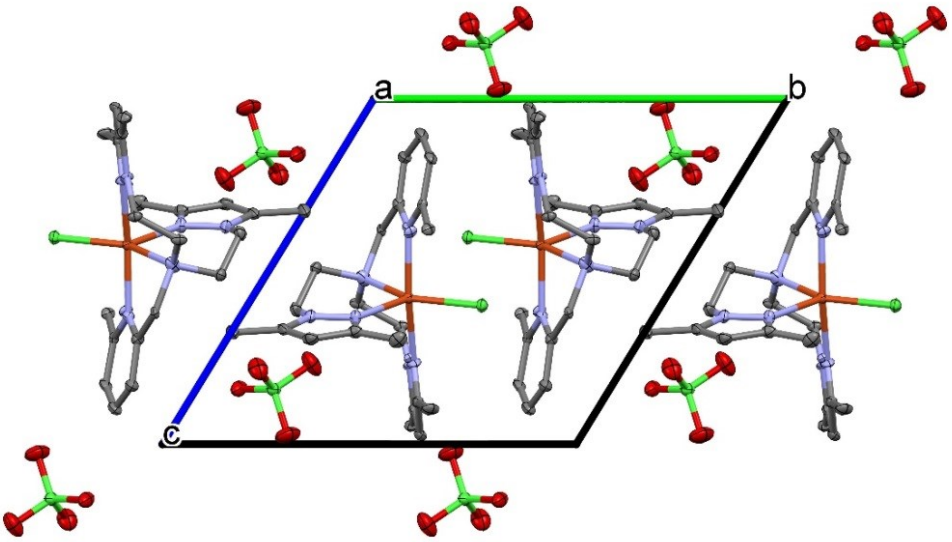


Fig. S1 Packing view of **1-ClO_4**

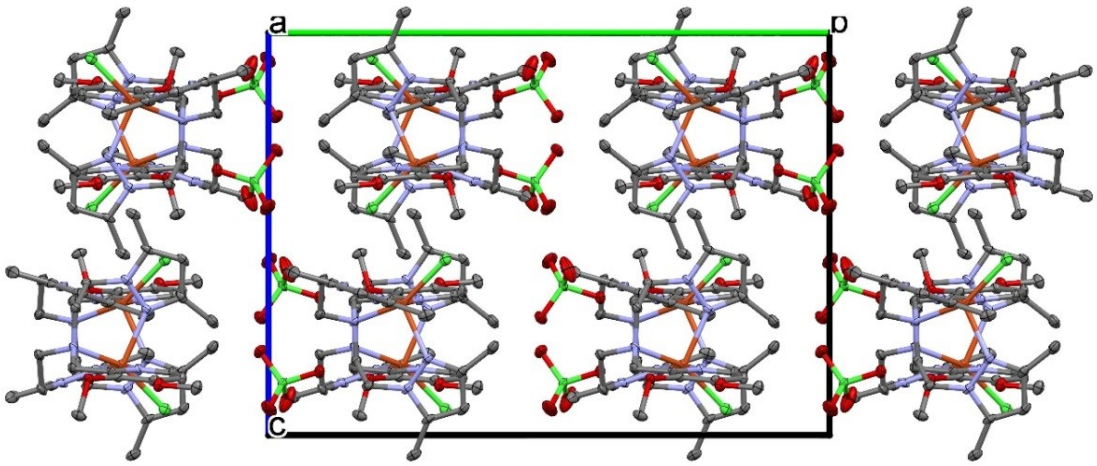


Fig. S2 Packing view of **2-ClO_4**

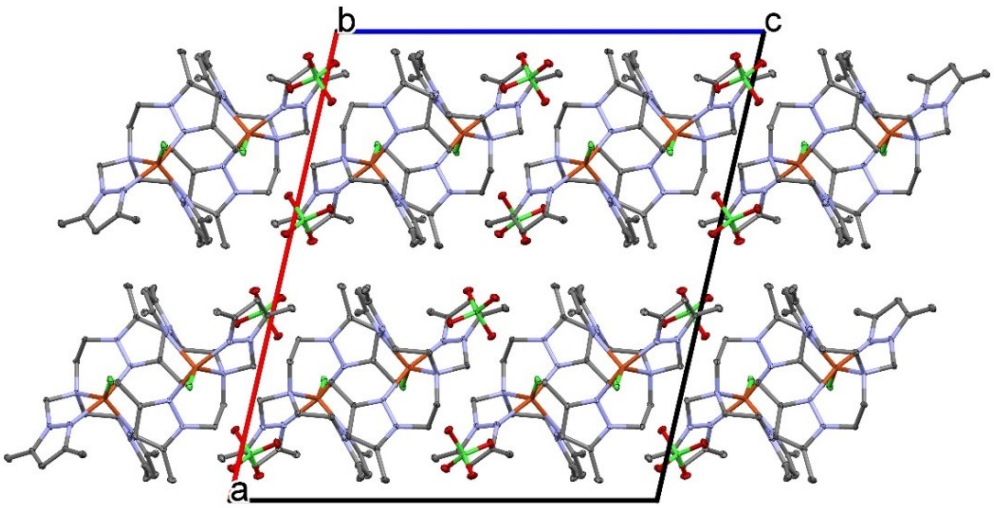


Fig. S3 Packing view of **4-ClO_4**

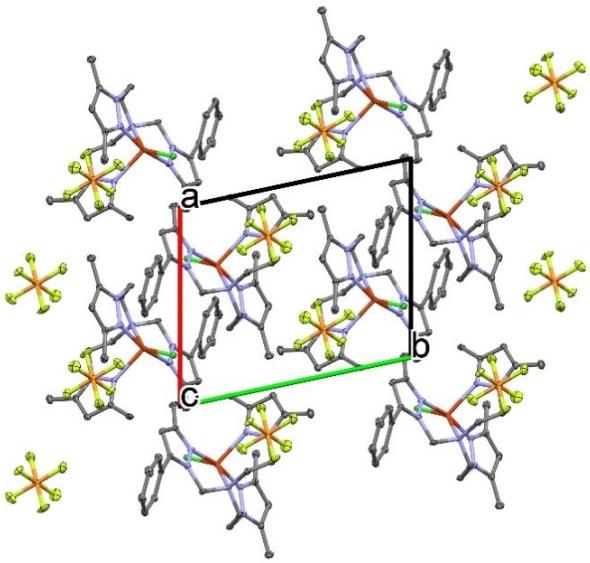


Fig. S4 Packing view of **5-PF_6**

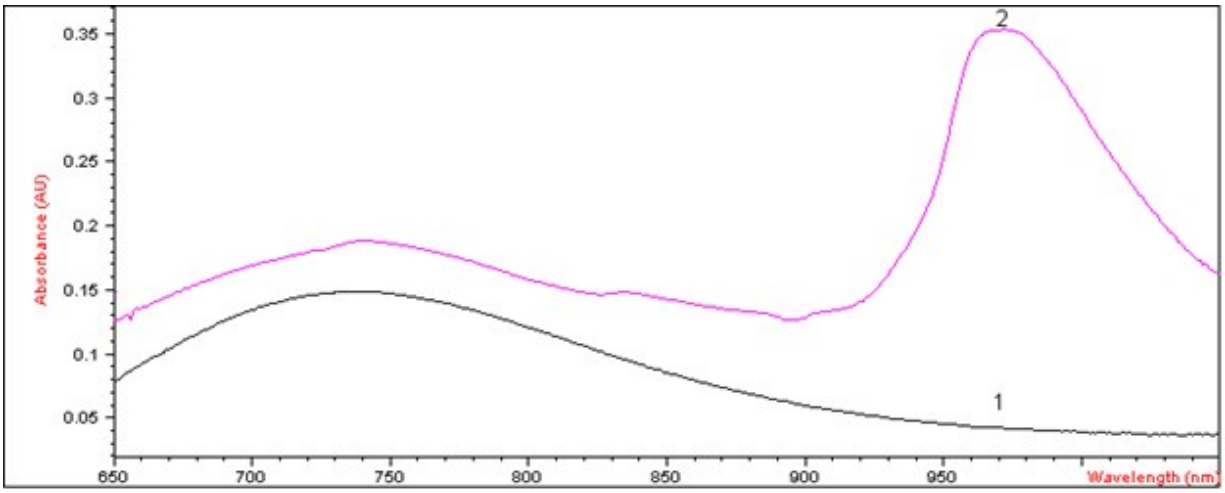


Fig. S5 Spectral changes of complex **1-PF_6** (6.95 x 10^{-4} M) in: (1) CH_3CN and (2) H_2O/CH_3CN solution (1:4, volume ratio) at room temperature.

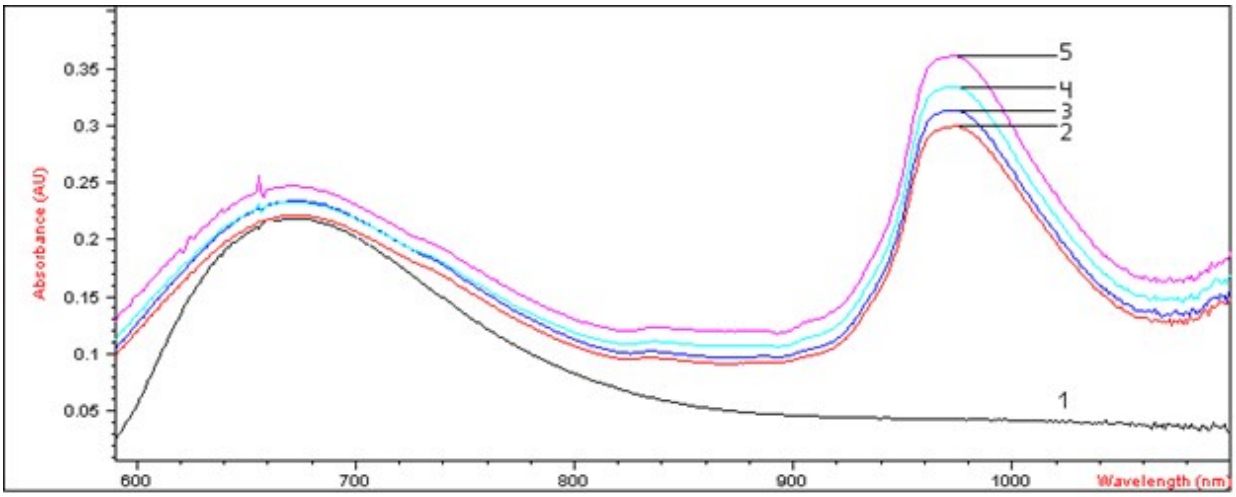


Fig. S6 Spectrophotometric titration of **2-ClO_4** (8.18 x 10^{-4} M) in H_2O/CH_3CN solutions (curve #, volume ratio) with increasing water contents: 1, 0/5 (black); 2, 0.30/5 (red); 3, 0.50/5 (blue); 4, 0.70/5 (turquoise); 5, 1.0/5 (purple) at room temperature.

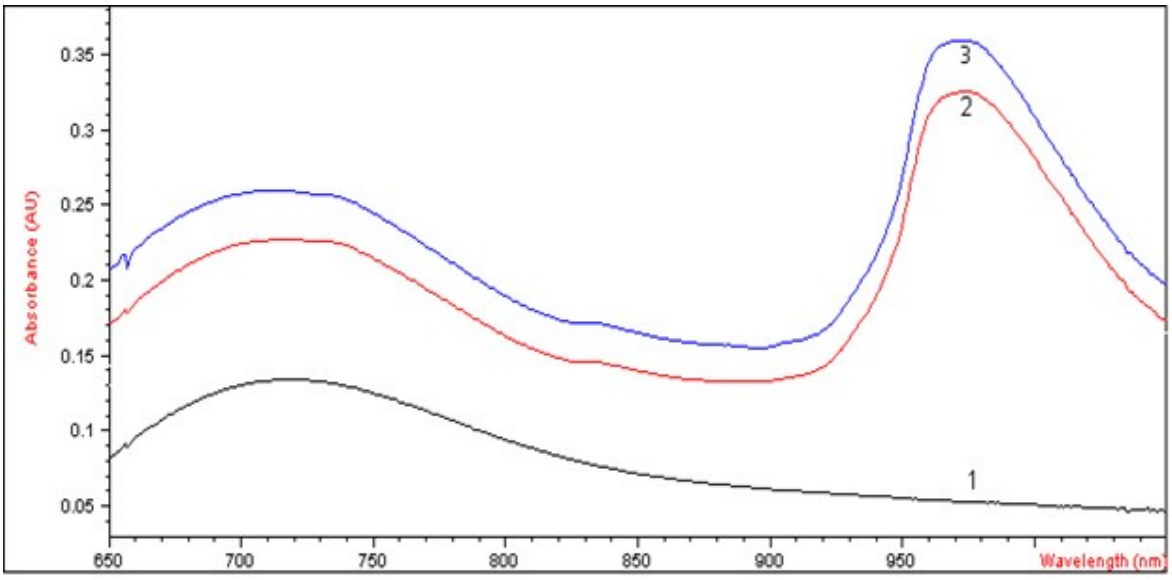


Fig. S7 Spectral changes of complex **4-PF_6** (8.21 x 10^{-4} M) in: (1) CH_3CN, (2) H_2O/CH_3CN (0.2:4.8) and (3) H_2O/CH_3CN (0.4:4.6) solution (v:v ratio) at room temperature.

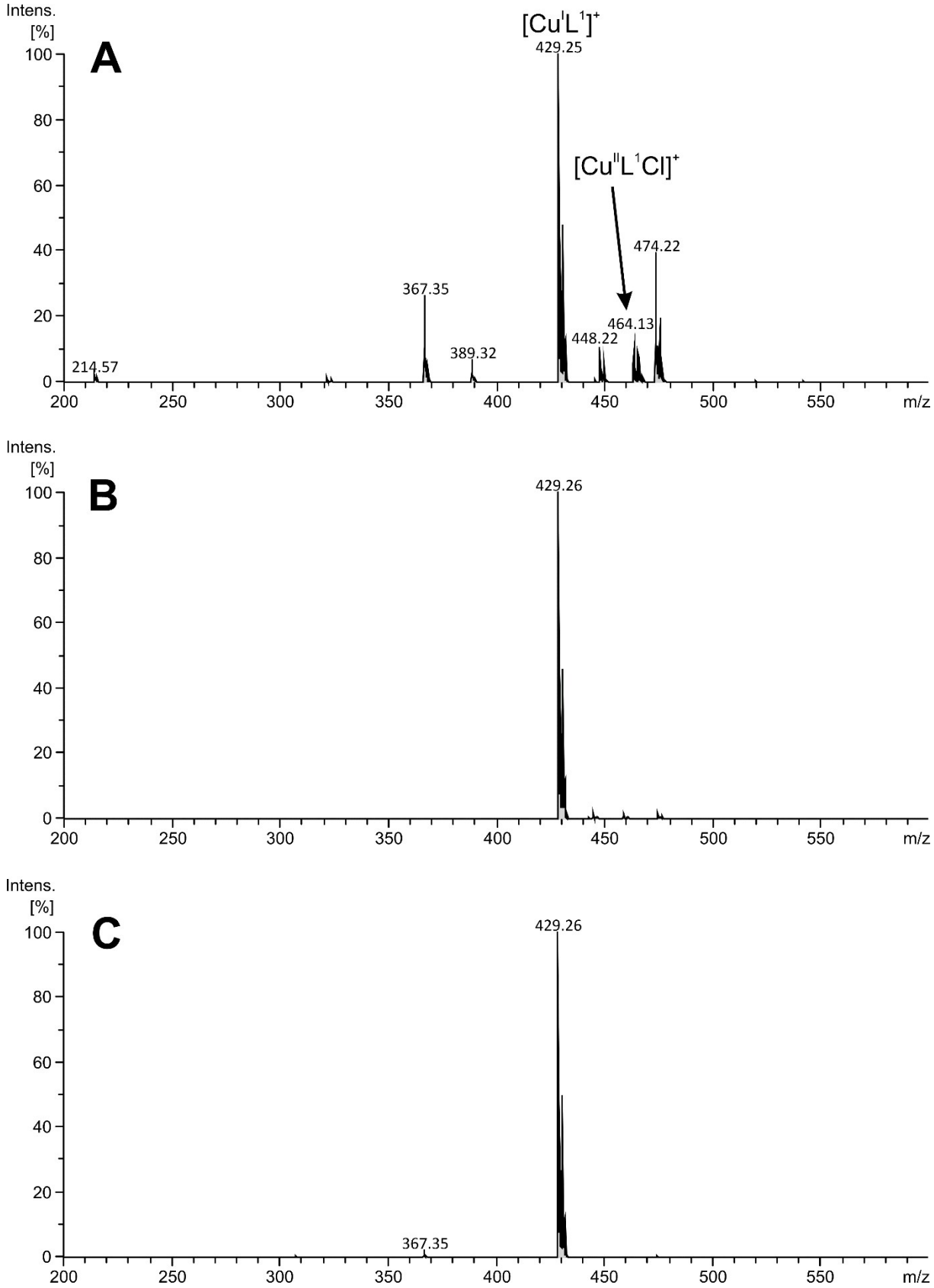


Fig. S8 The ESI-MS spectra of samples containing the $[Cu(L^1)Cl]PF_6$ (**1-PF$_6$**) (panel **A**), mixture of (1) at 10 μM and 290 μM L-Cys after 60 h of interaction (panel **B**), mixture of (1) at 10 μM and 290 μM GSH after 60 h of interaction (panel **C**).

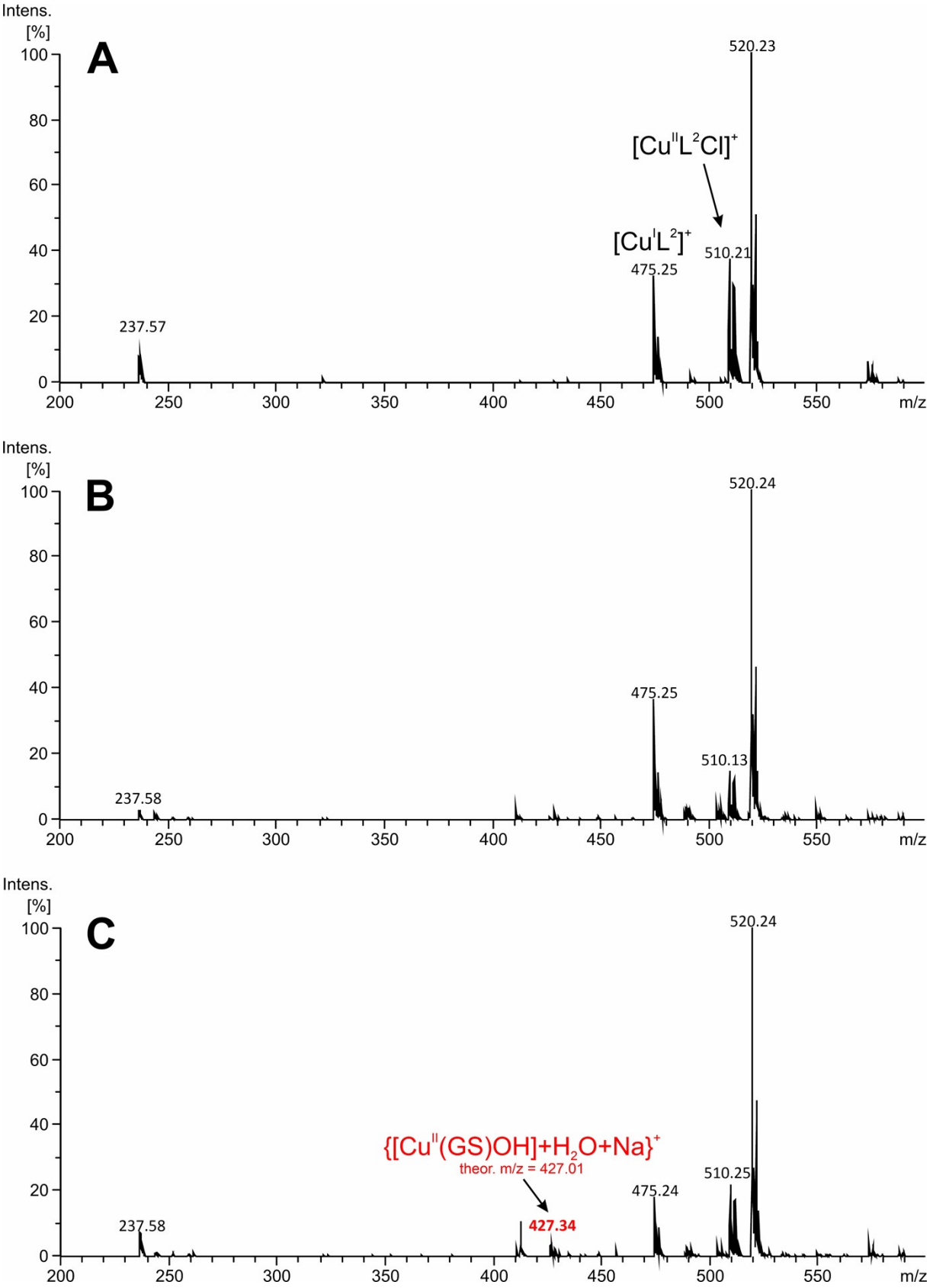


Fig. S9 The ESI-MS spectra of samples containing the $[Cu(L^2)Cl]ClO_4$ (**2-ClO$_4$**) (panel **A**), mixture of (2) at 10 μM and 290 μM L-Cys after 60 h of interaction (panel **B**), mixture of (2) at 10 μM and 290 μM GSH after 60 h of interaction (panel **C**).

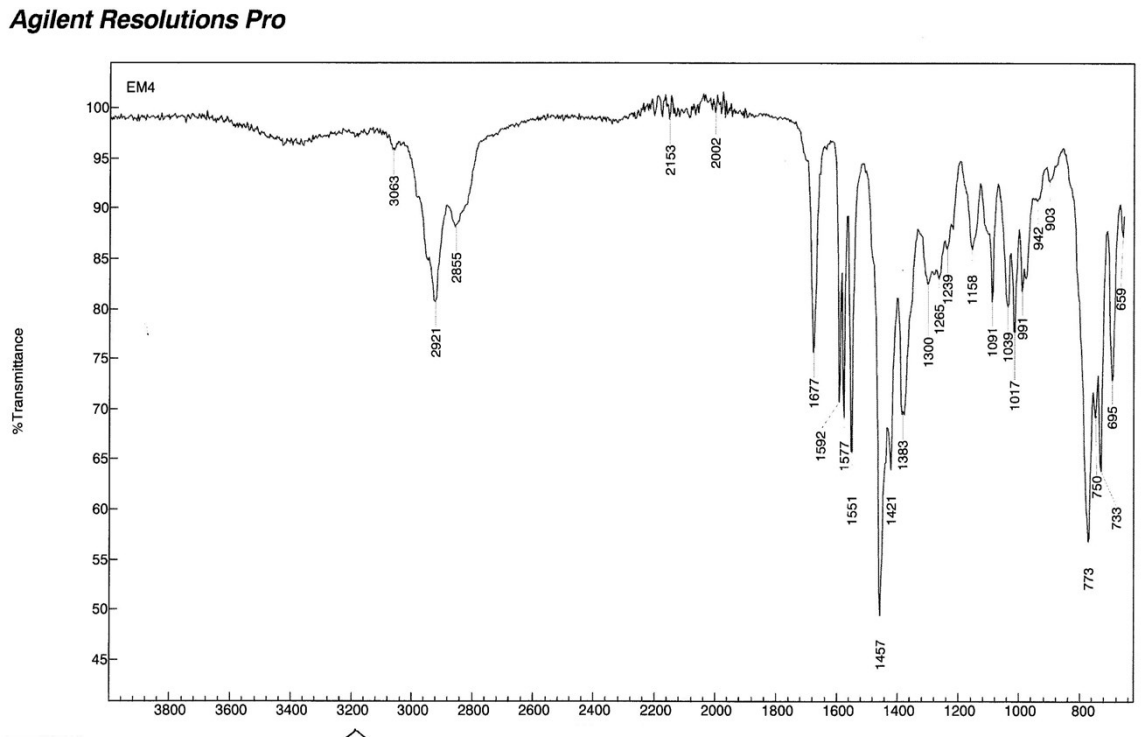


Fig. S10 Solid IR spectrum of **L[1]**.

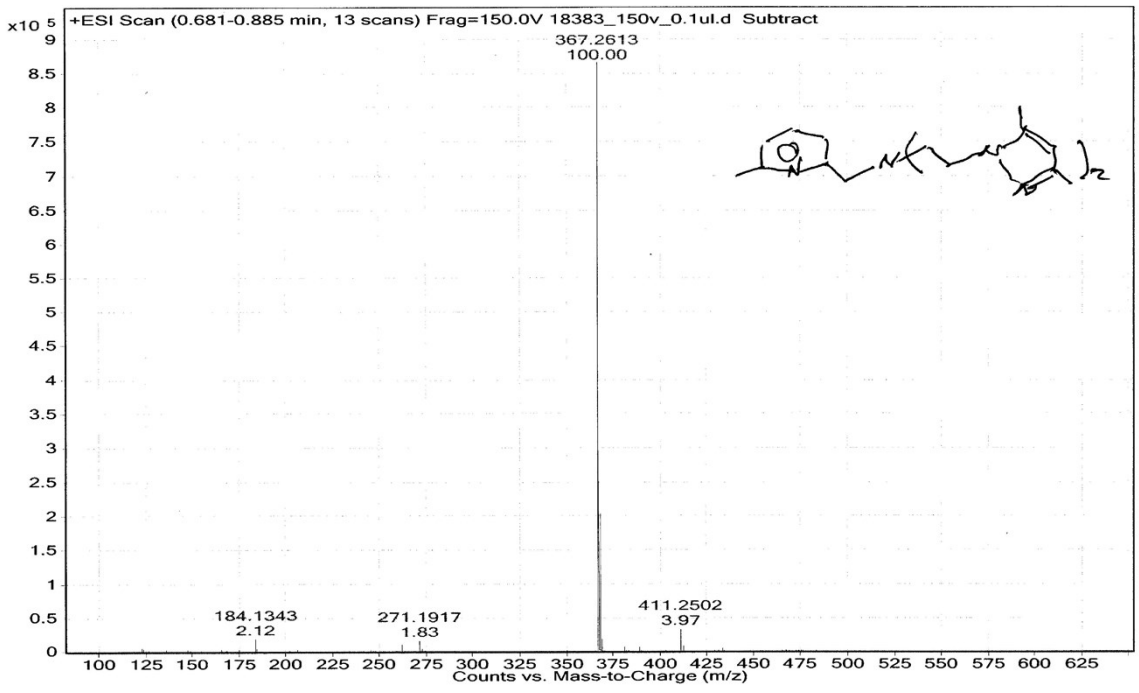
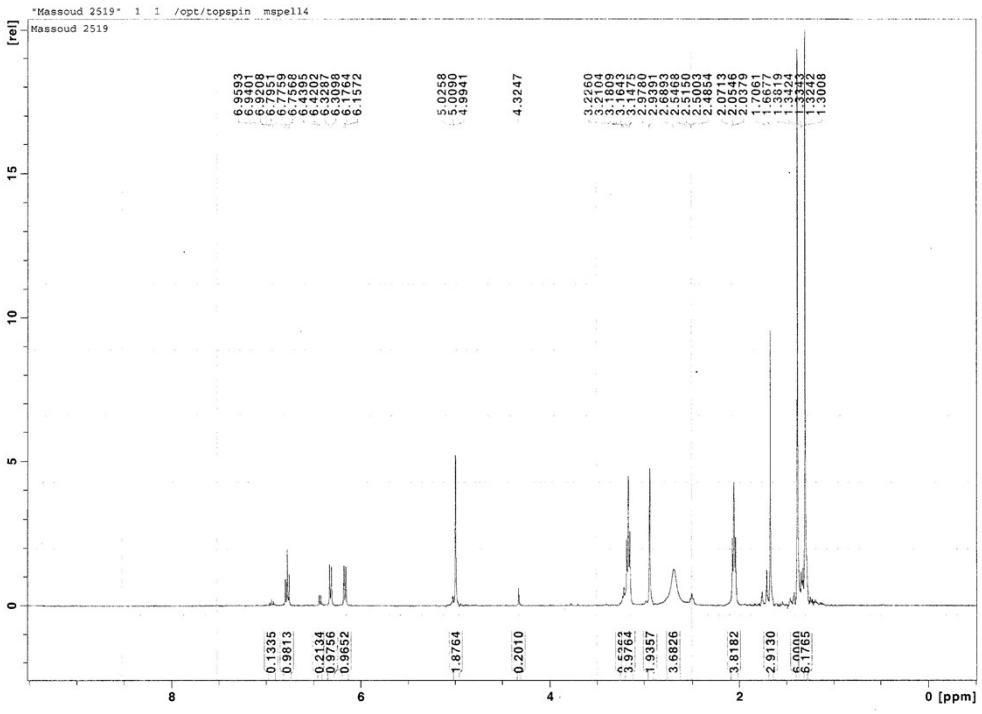


Fig. S11 ESI-MS of **L[1]** in MeOH.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1.6677
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1.3242
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4
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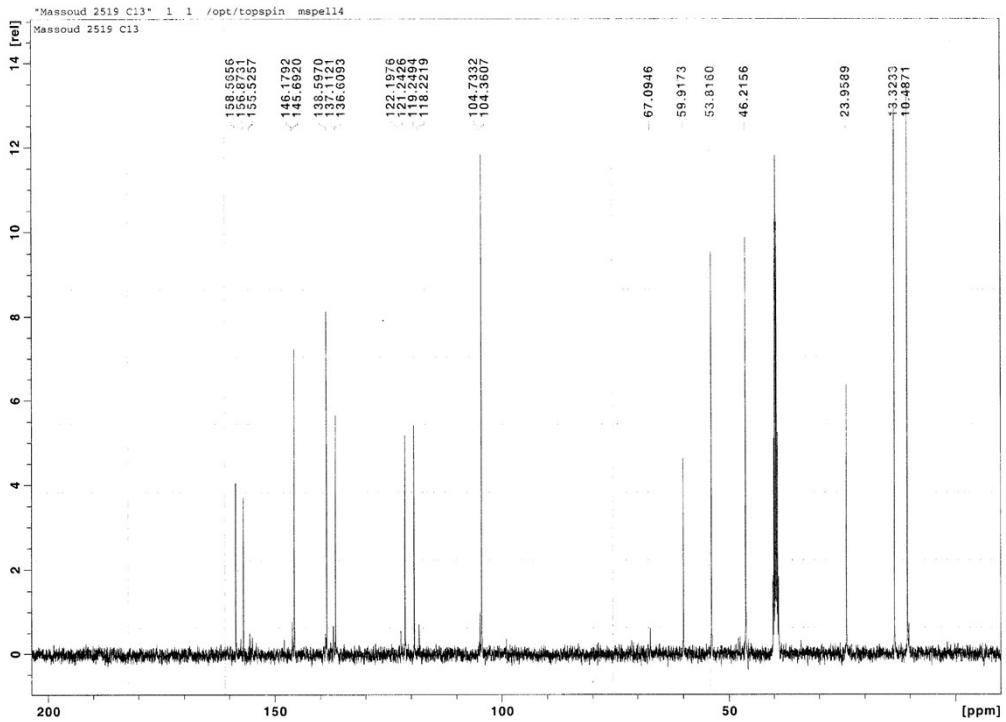
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50
[ppm]

Fig. S12 ^{1}H (top) and ^{13}C (bottom) NMR spectra of **L[1]** in DMSO-d_6

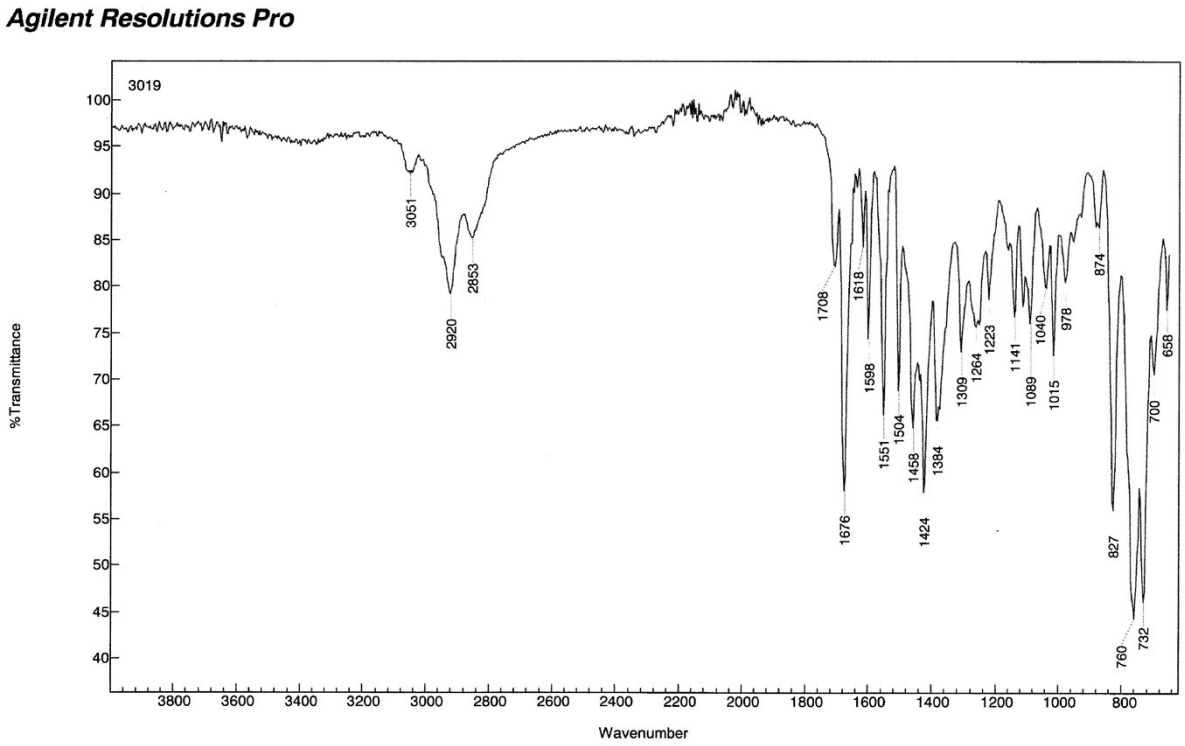

Fig. S13 Solid IR spectrum of **L[3]**.

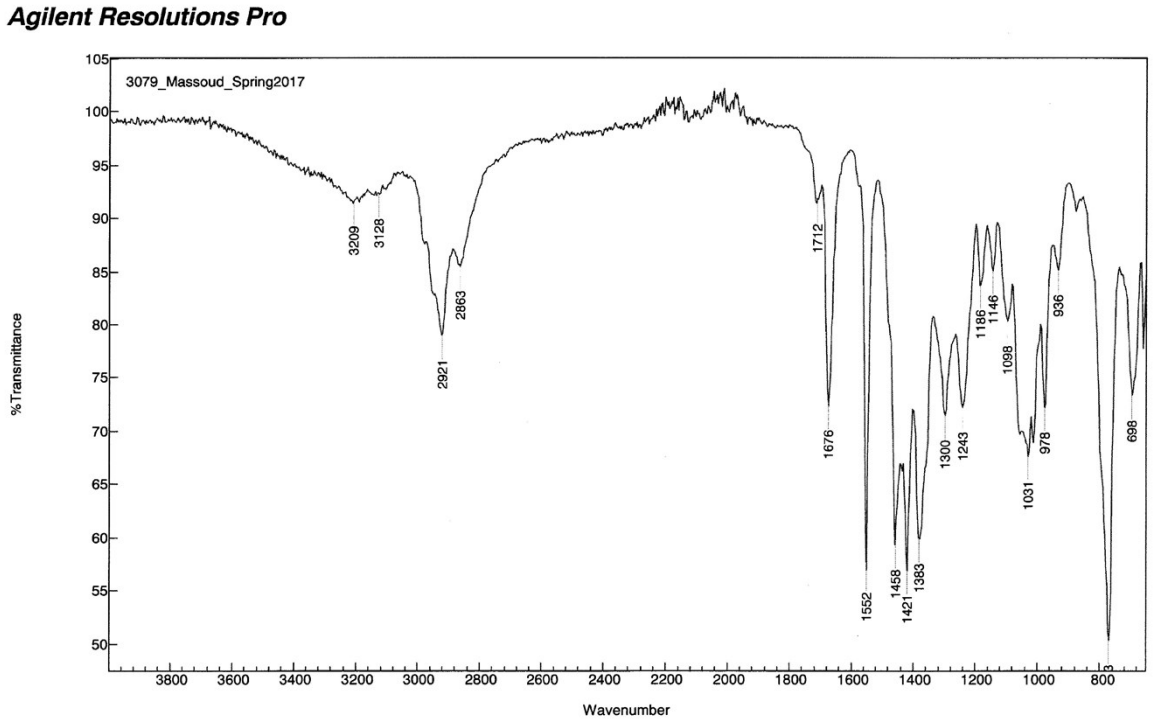

Fig. S14 Solid IR spectrum of **L[4]**.

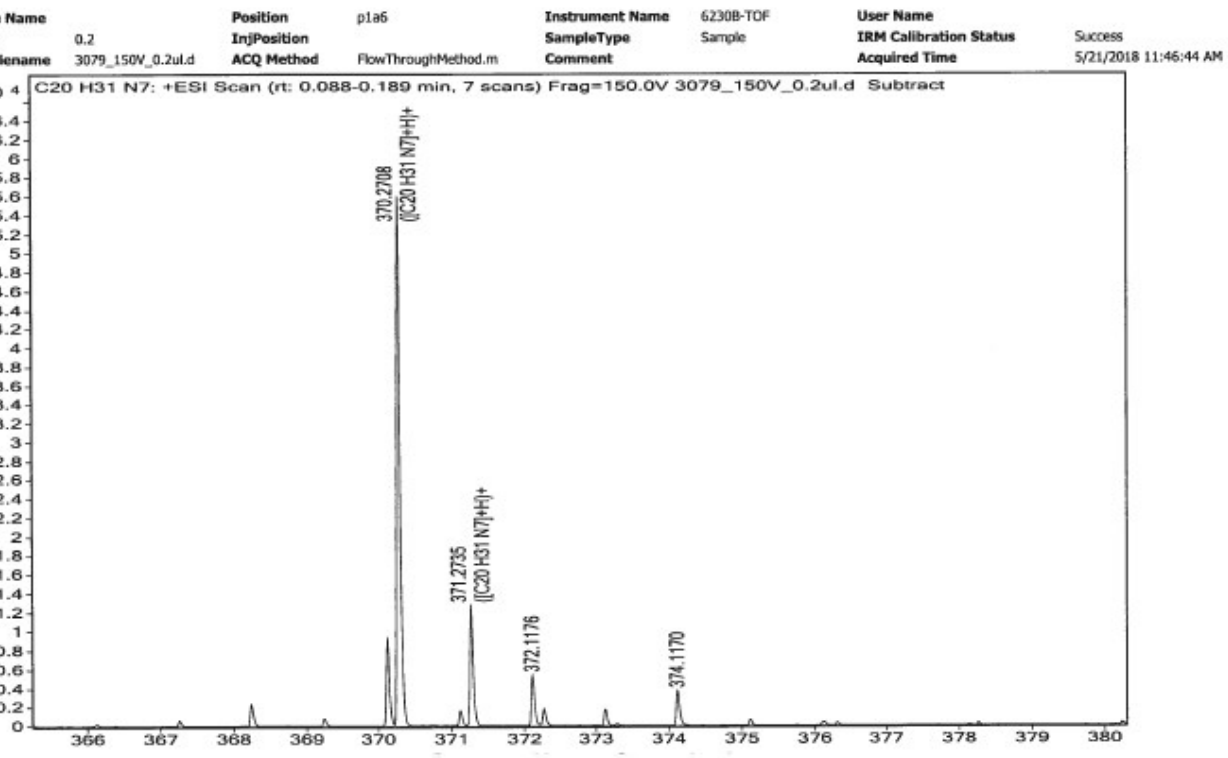

Fig. S15 ESI-MS of **L[4]** in MeOH

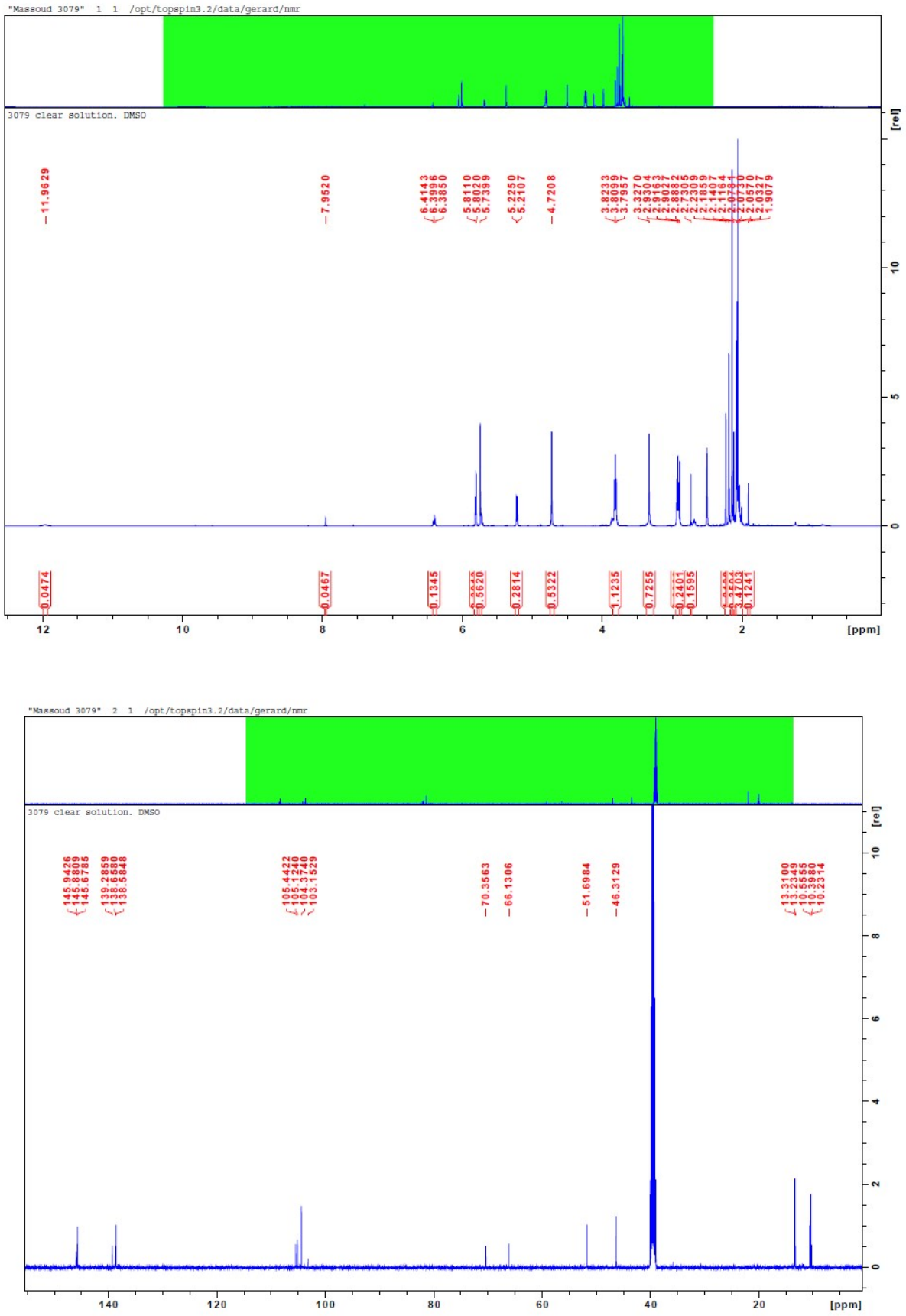

Fig. S16 ^{1}H (top) and ^{13}C (bottom) NMR spectra of **L^{4}** in DMSO-d_6

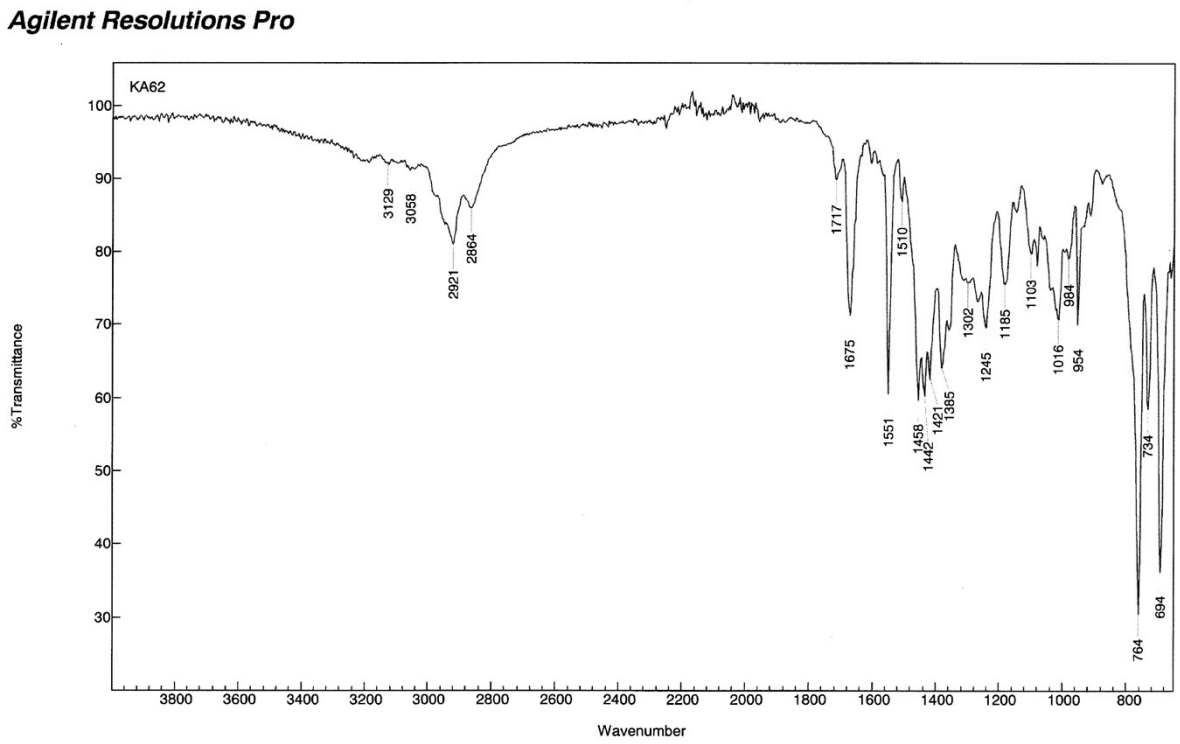

Fig. S17 Solid IR spectrum of **L**^{5}.

Sample Name		Position	p1d2	Instrument Name	6230B-TOF	User Name	
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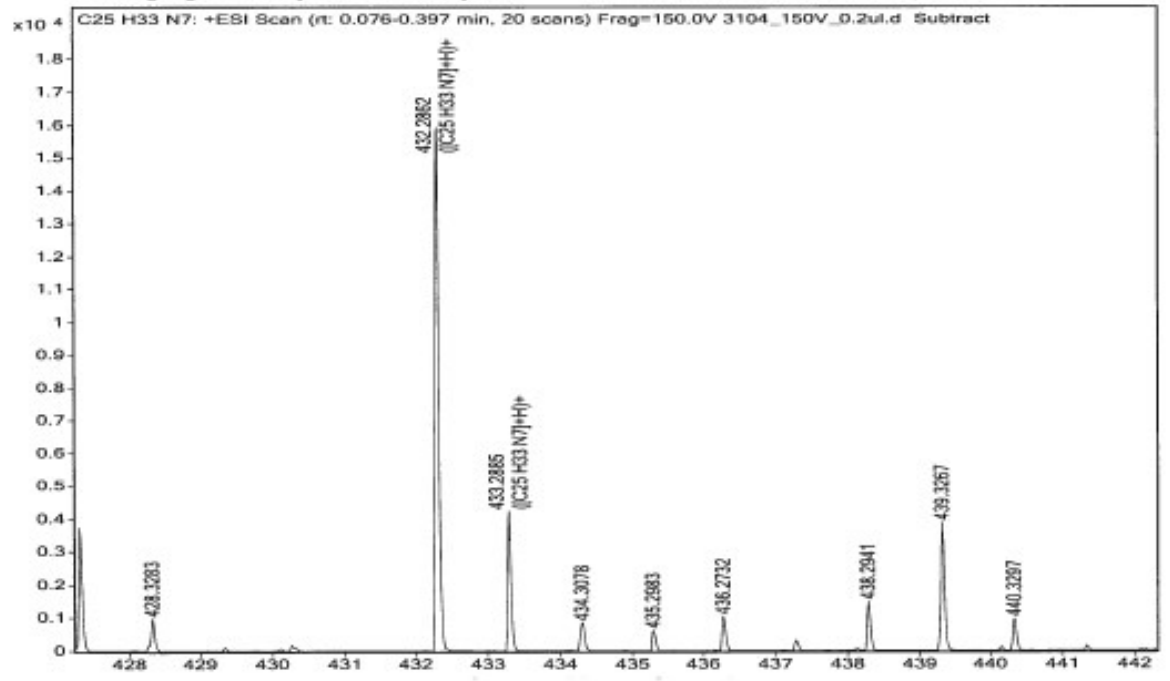

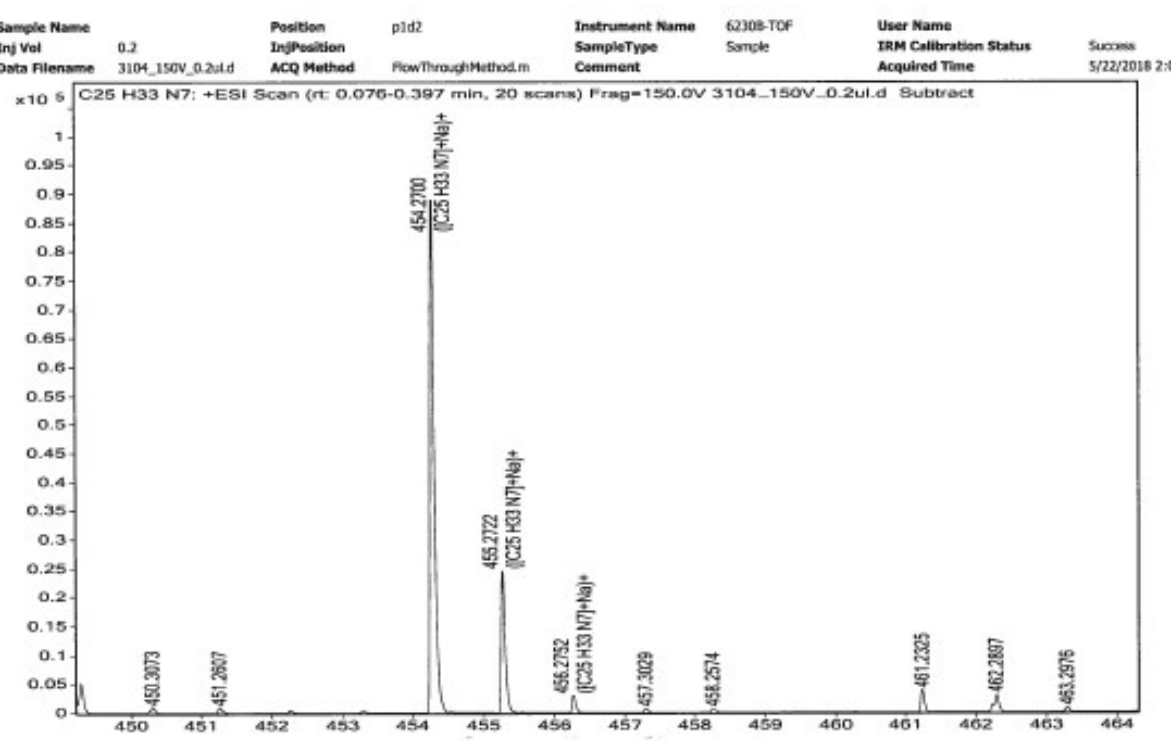

Fig. S18 ESI-MS of **L[5]** in MeOH

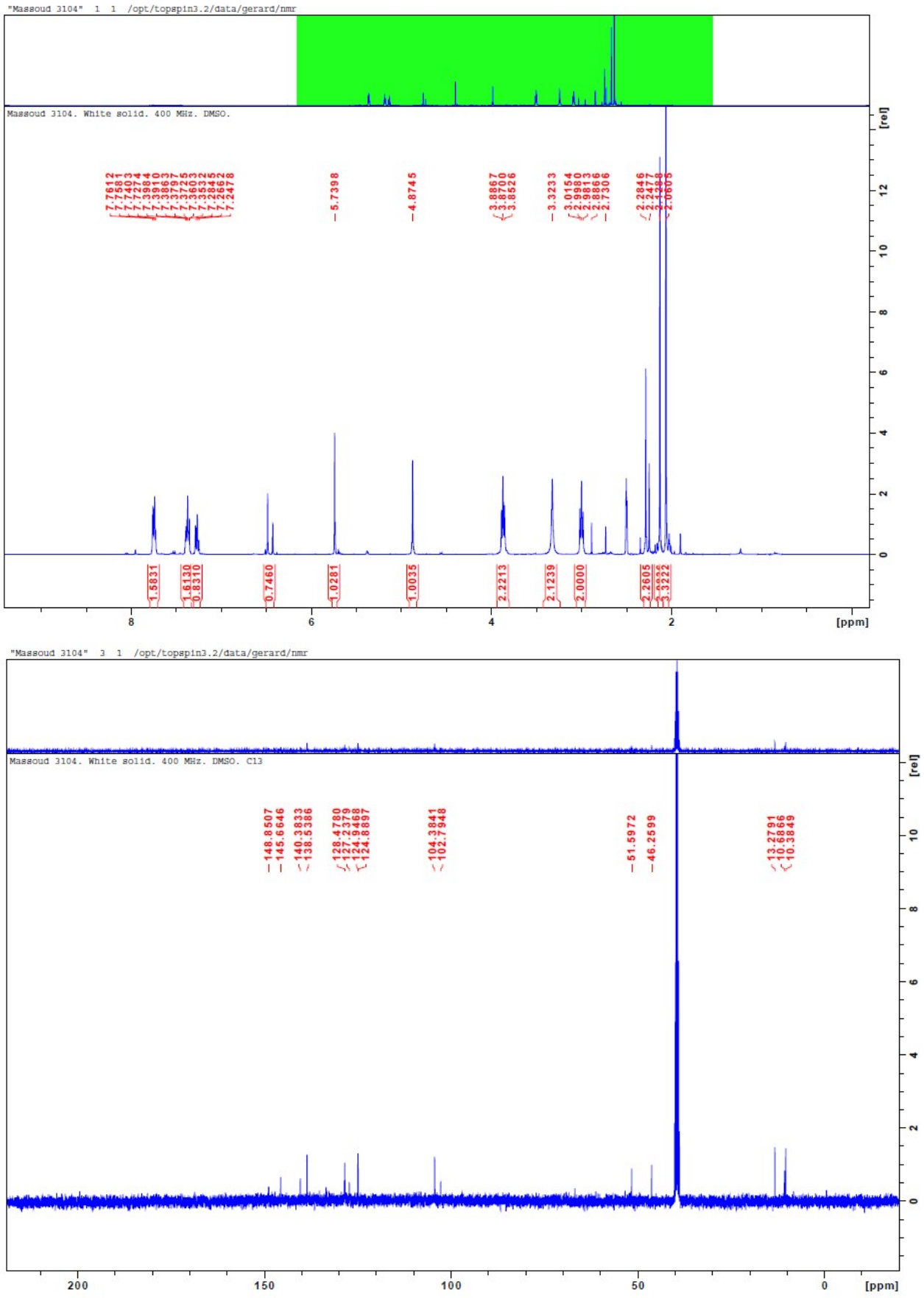

Fig. S19 ^{1}H (top) and ^{13}C (bottom) NMR spectra of **L^{5}** in DMSO-d_6

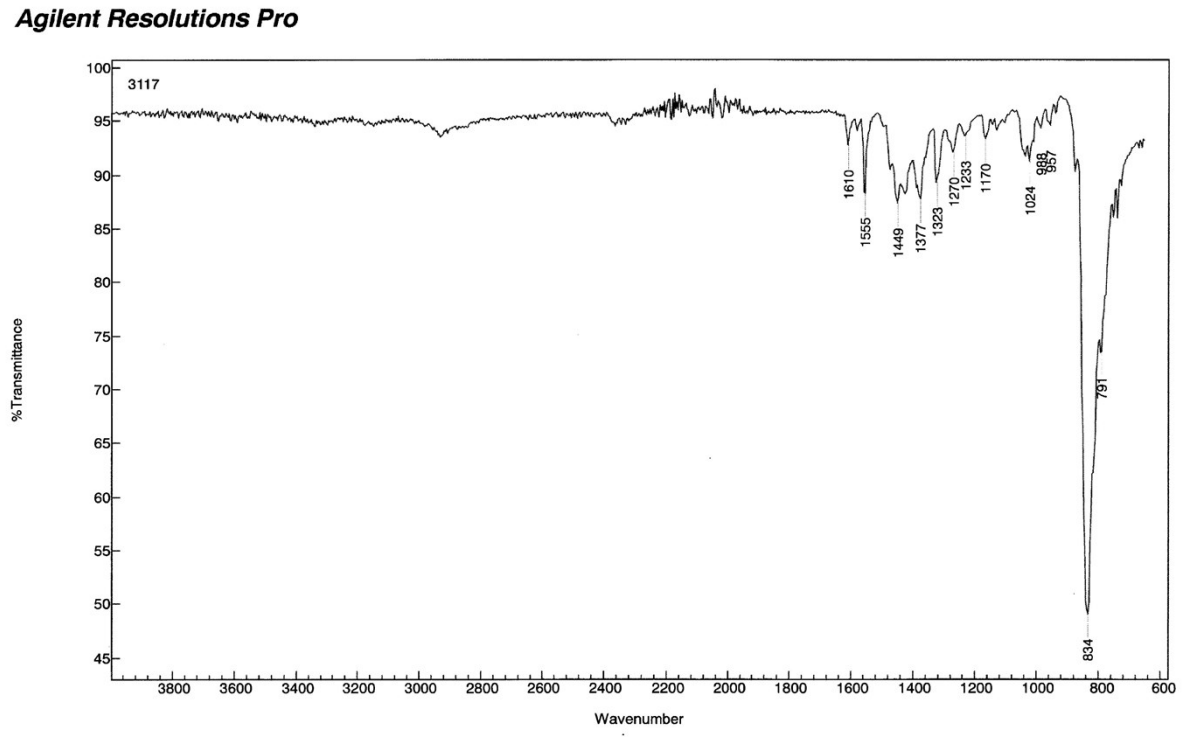

Fig. S20 Solid IR spectrum of complex **1-PF$_6$**.

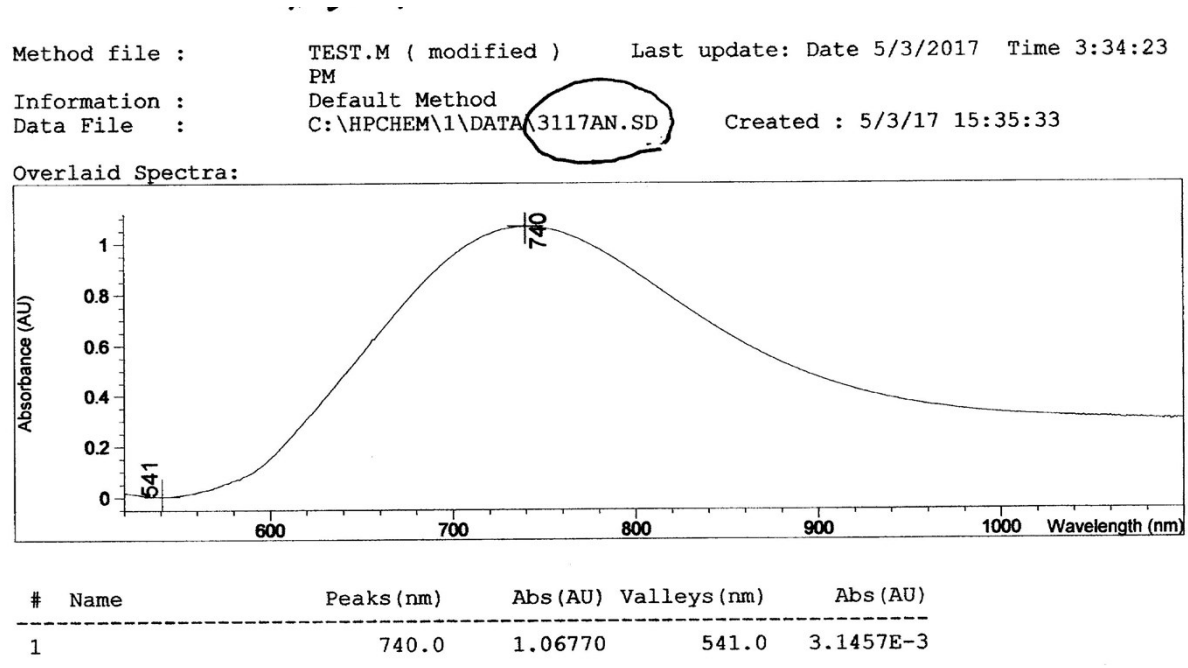

Fig. S21 Electronic spectrum of complex **1-PF$_6$** (4.652 x 10^{-3} M) in acetonitrile.

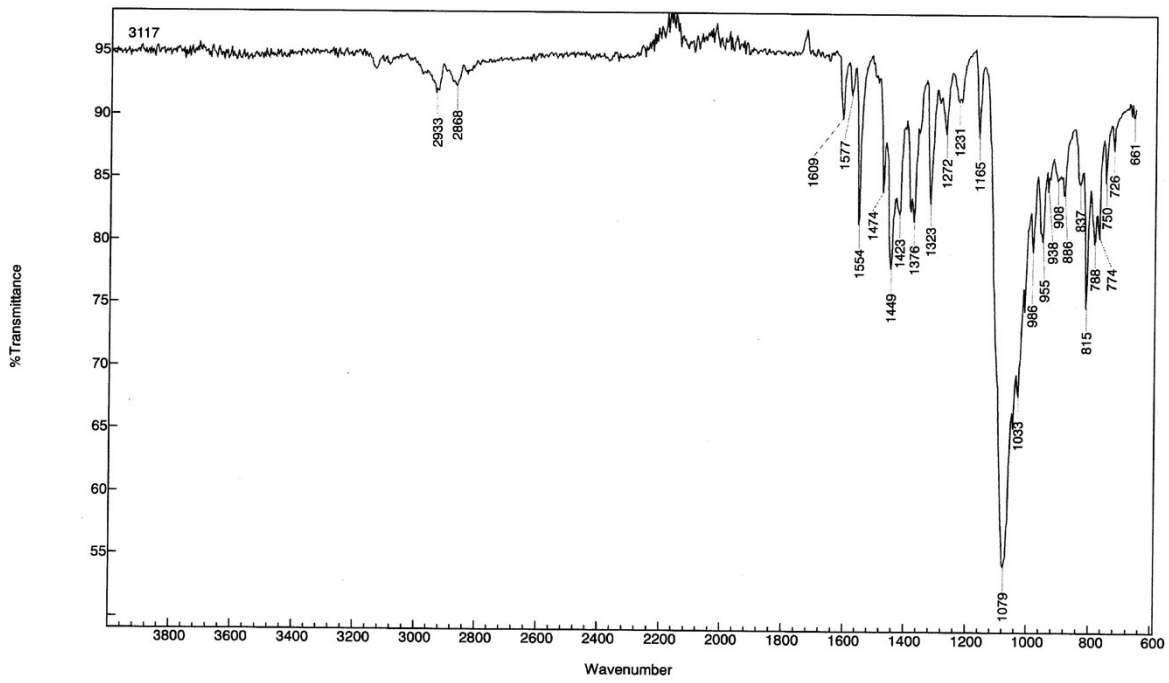

Fig. S22 Solid IR spectrum of complex **1-ClO_4**.

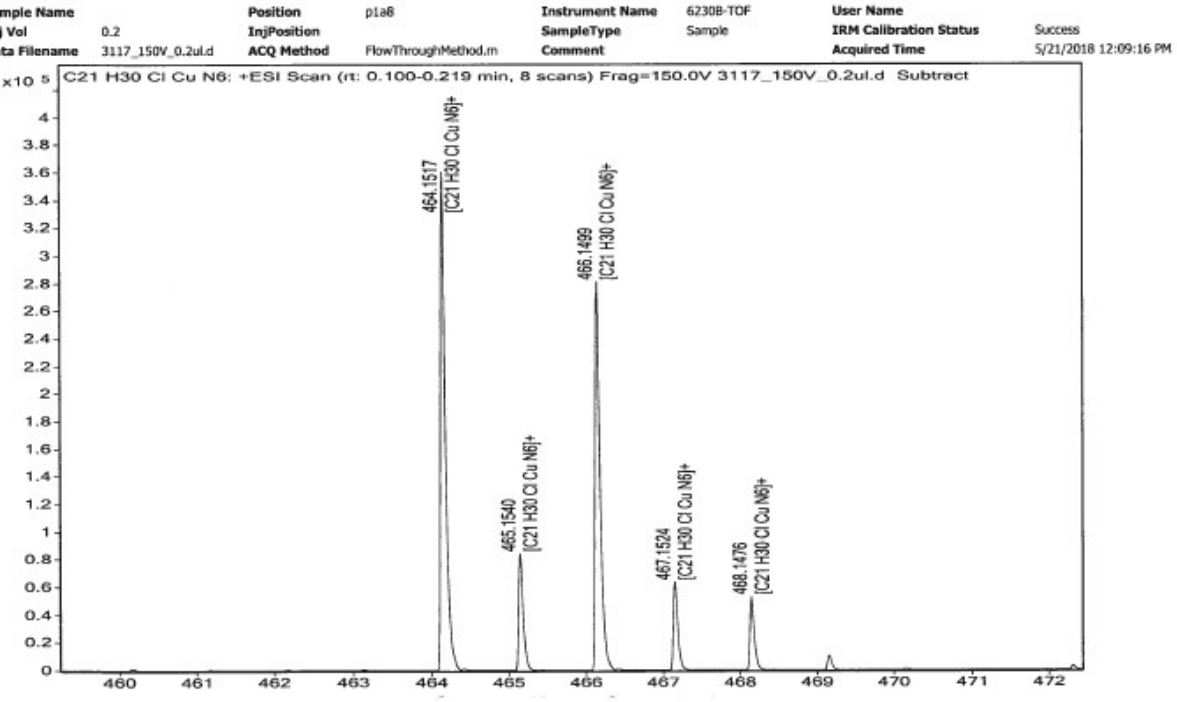

Fig. S23 ESI-MS of complex **1-ClO_4** in CH_3CN.

2 mon green

Conductivity: 334 µS/cm

Method file : 3510.M (modified) Last update: Date 4/21/2021 Time 11:46:52 AM

Information : Default Method

Data File : C:\HPCHEM\1\DATA\2ANMD.SD Created : 4/21/21 11:46:11

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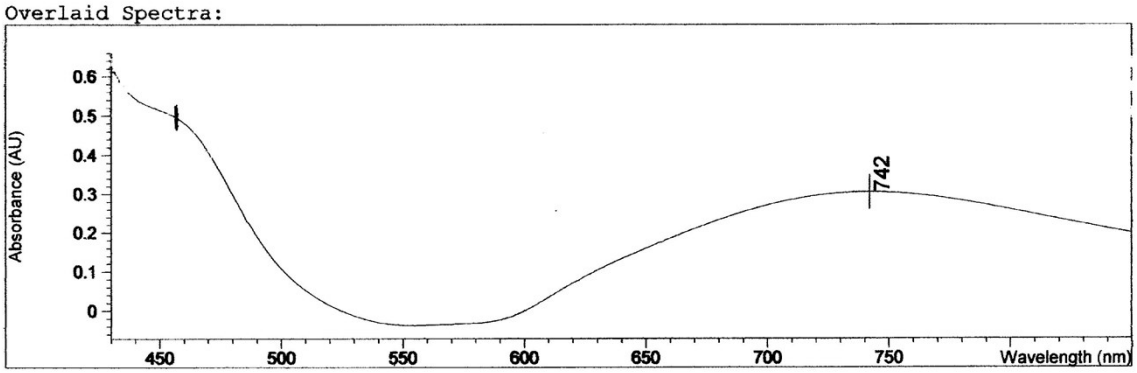

#	Name	Peaks(nm)	Abs(AU)
1		742.0	0.30485
1		***	***
Shoulder		449	0.516797

Fig. S24 Electronic spectrum of complex **1-ClO_4** (2.036 x 10^{-3} M) in CH_3CN.

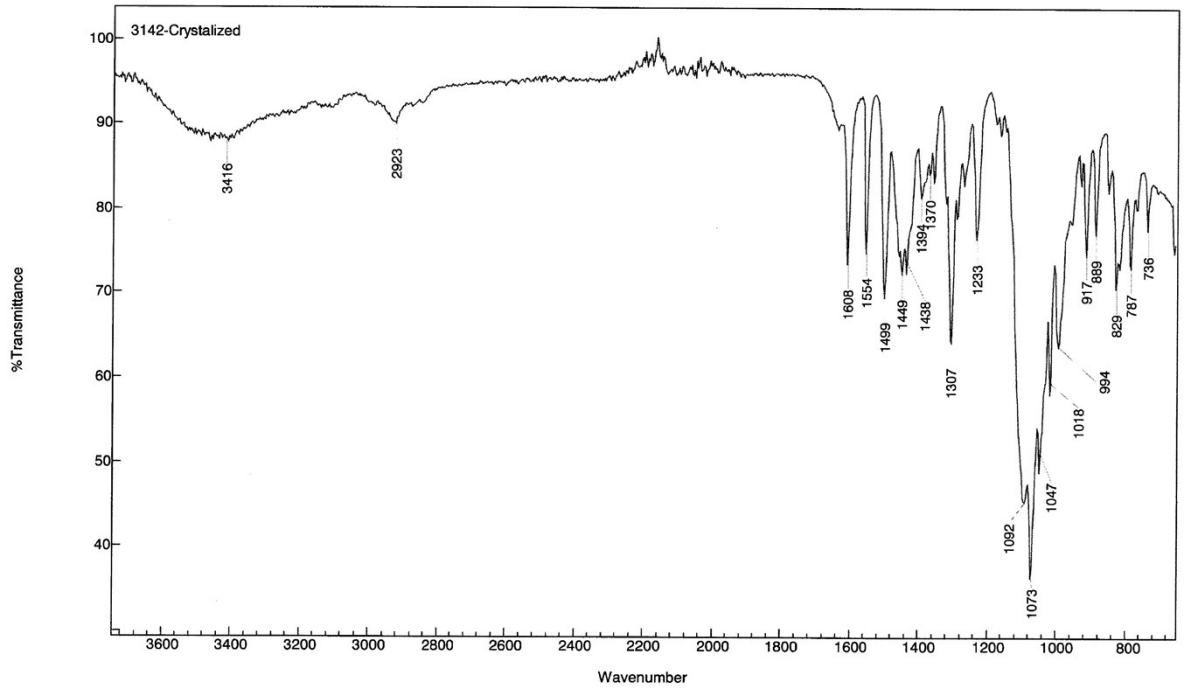

Fig. S25 Solid IR spectrum of complex **2-ClO_4**.

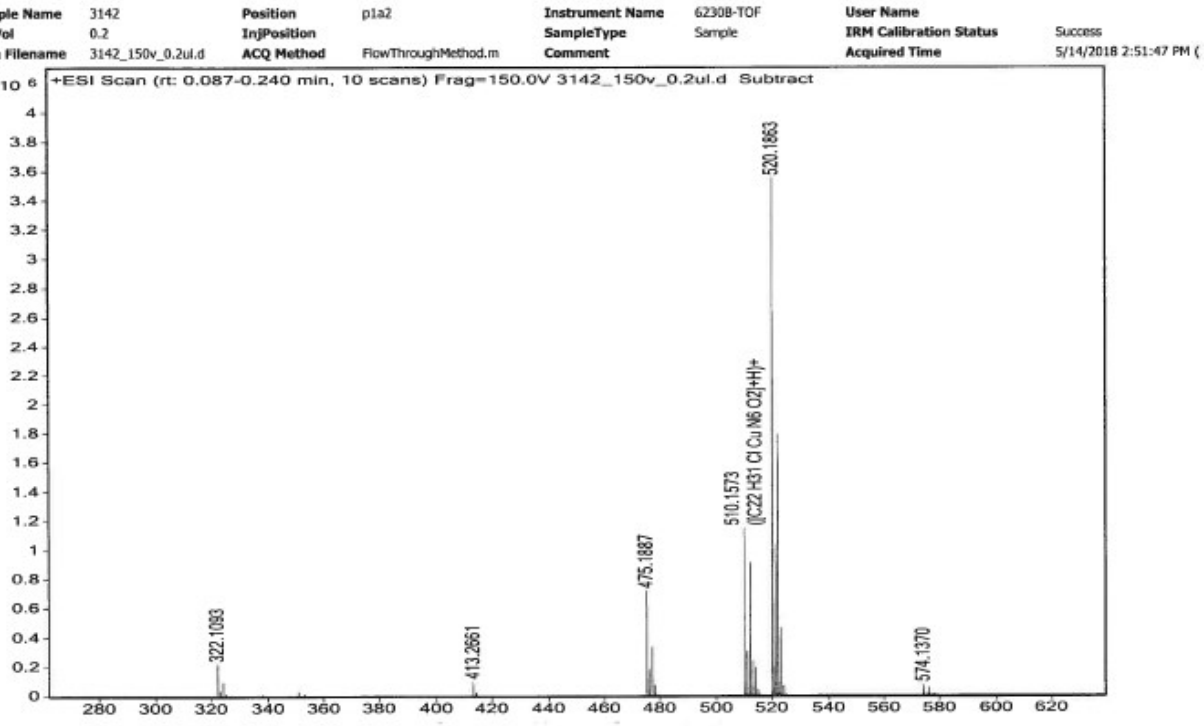

Fig. S26 ESI-MS of complex **2-ClO_4** in CH_3CN.

Spectrum/Peak Report Date 5/31/2017 Time 12:02:06 Page 1 of 1

Method file : TEST.M (modified) Last update: Date 5/31/2017 Time 12:01:59 PM
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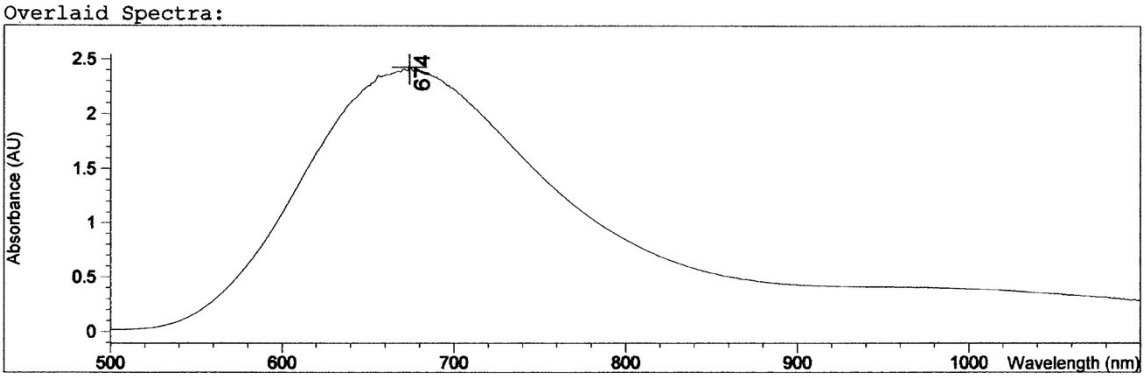


#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1		674.0	2.42510	***	***

Fig. S27 Electronic spectrum of complex **2-ClO$_4$** (9.640 x 10^{-3} M) in CH_3CN.

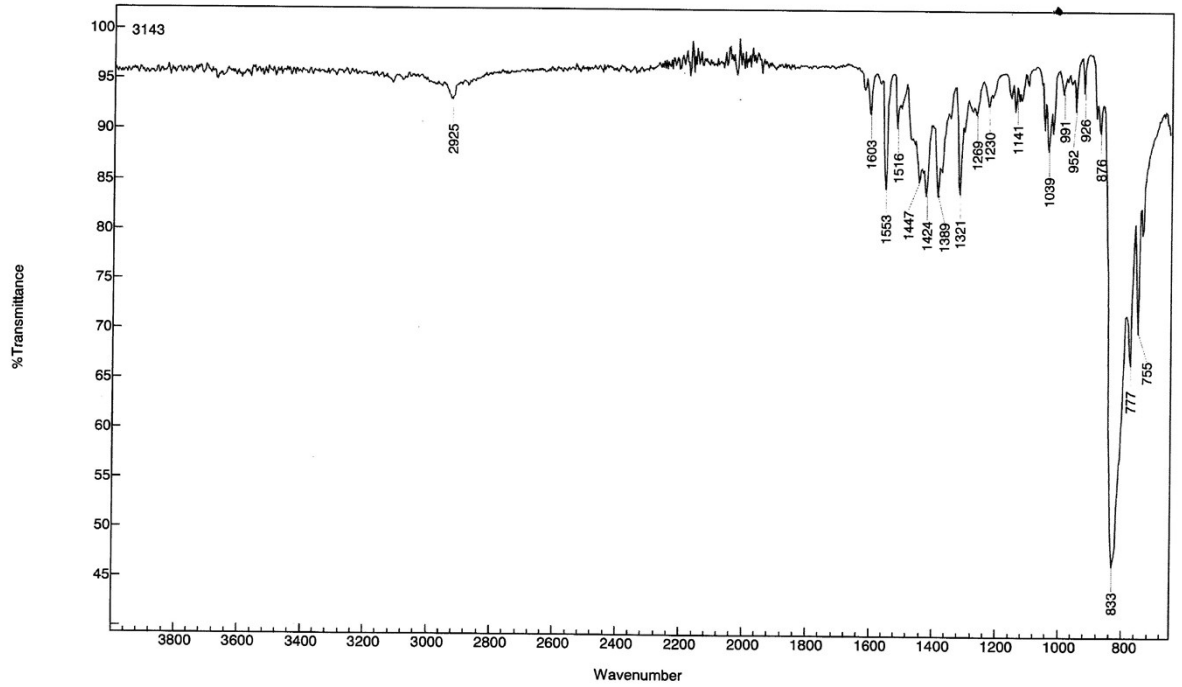


Fig. S28 Solid IR spectrum of complex **3-PF$_6$**.

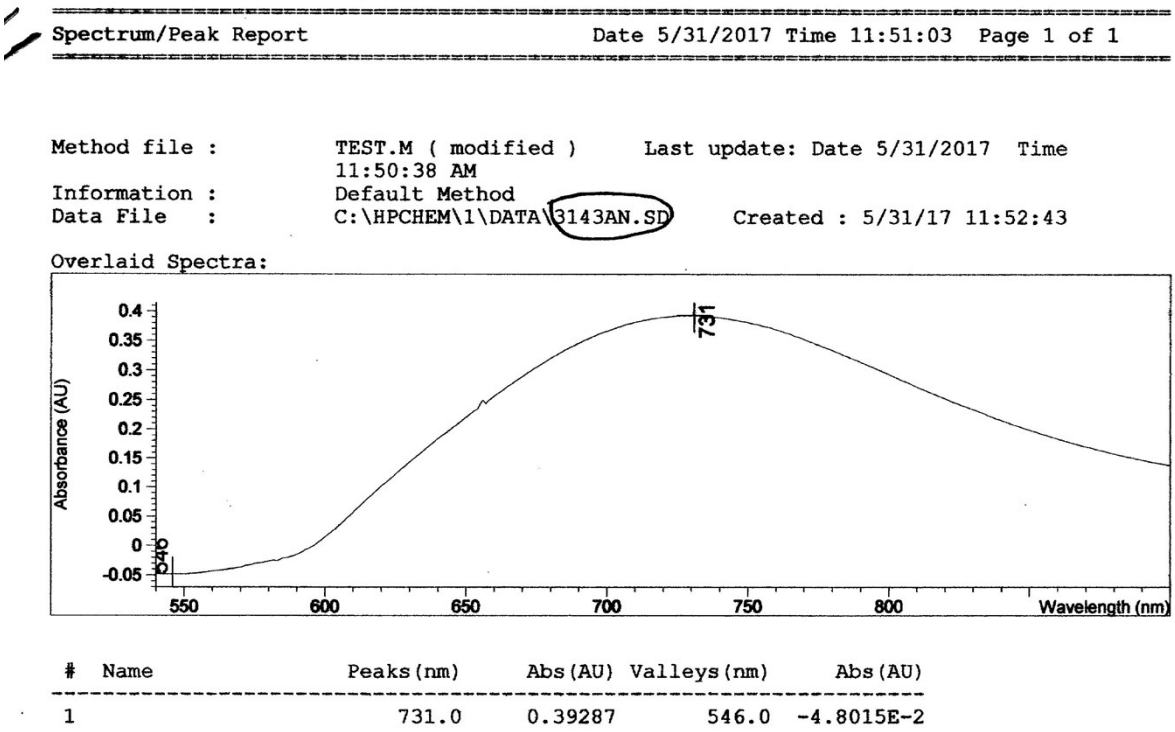


Fig. S29 Electronic spectrum of complex **3-PF$_6$** (1.655 x 10^{-3} M) in CH_3CN.

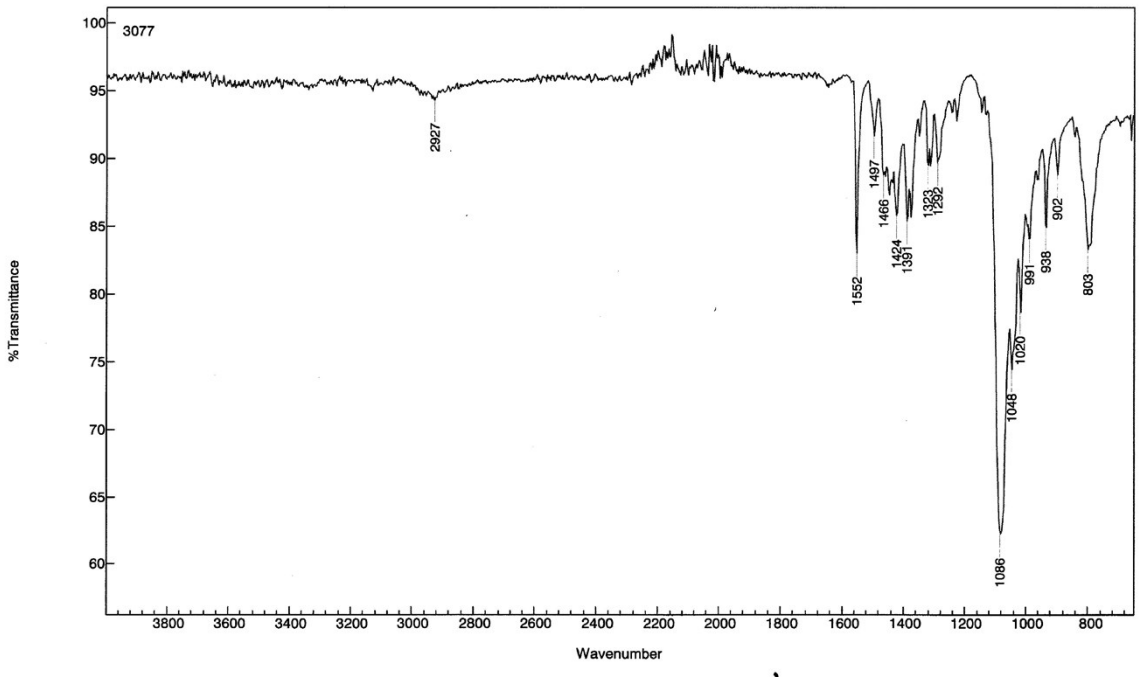


Fig. S30 Solid IR spectrum of complex **4-ClO$_4$**.

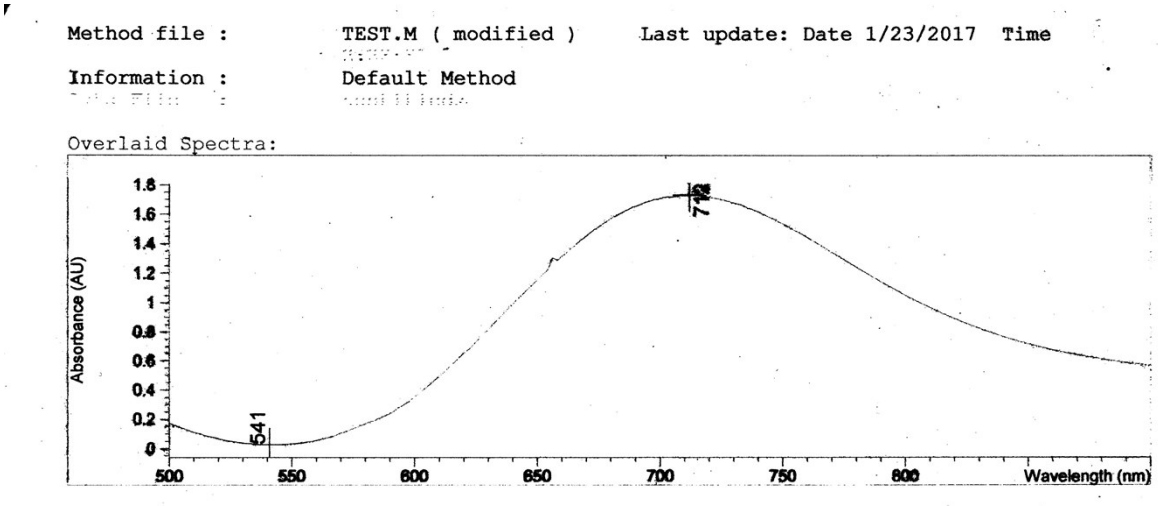


Fig. S31 Electronic spectrum of complex **4-ClO$_4$** (7.085 x 10^{-3} M) in CH_3CN

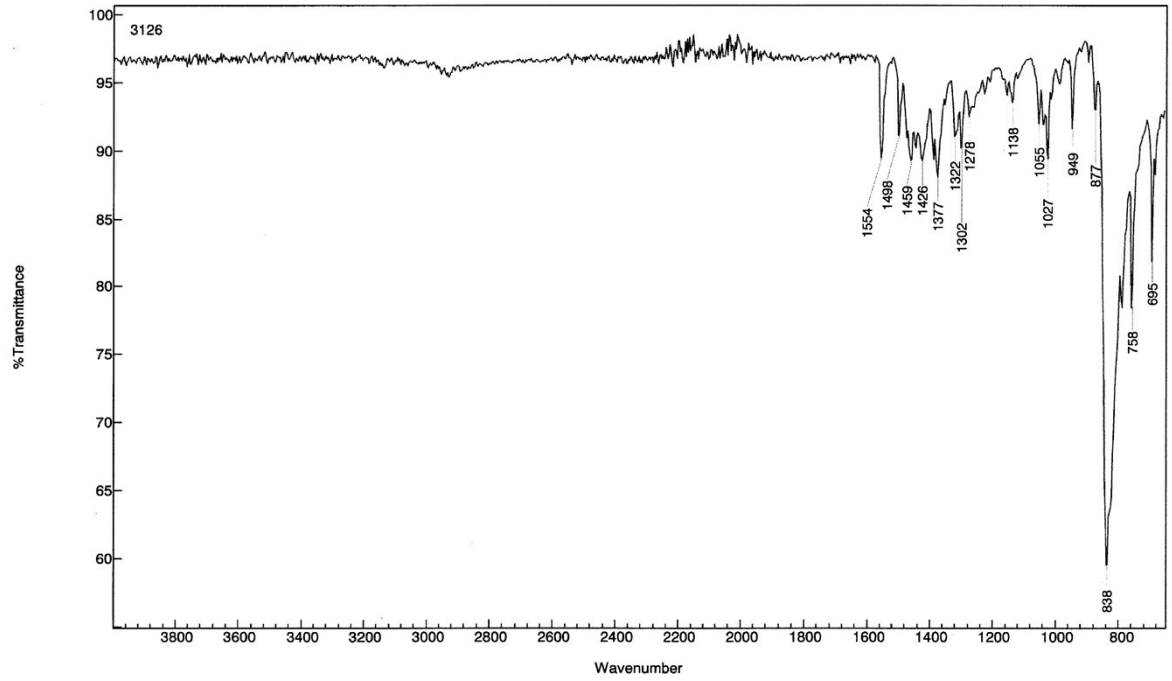


Fig. S32 Solid IR spectrum of complex **5-PF_6**.

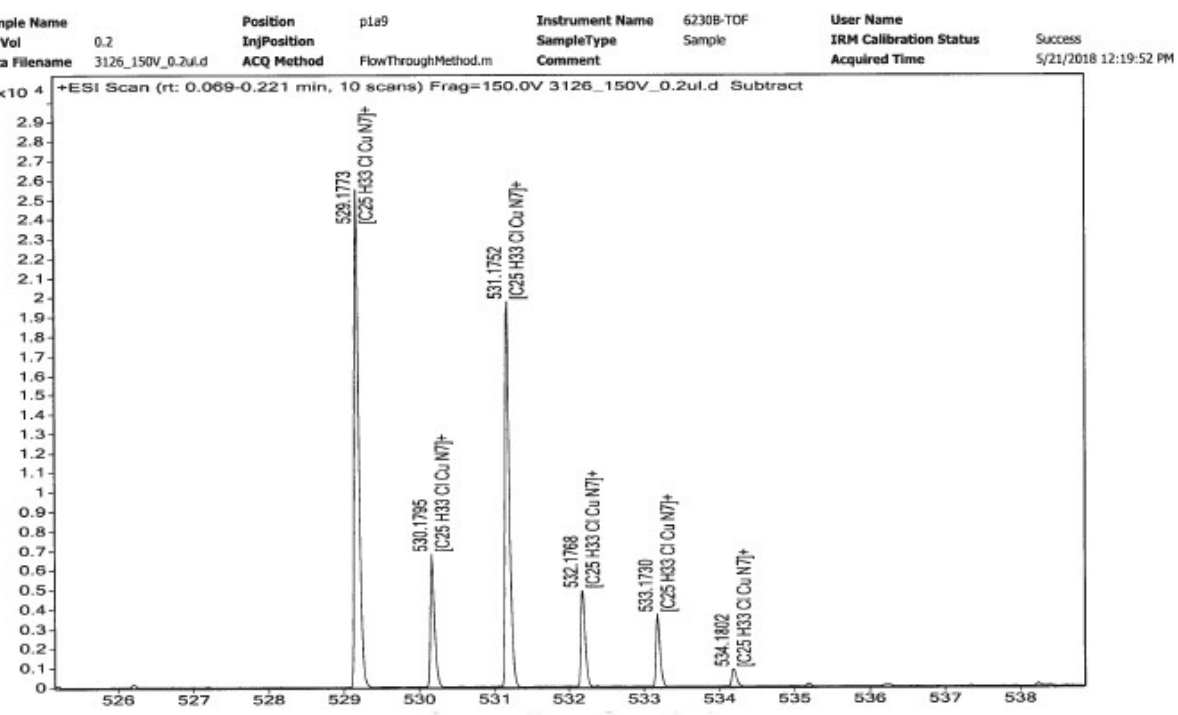


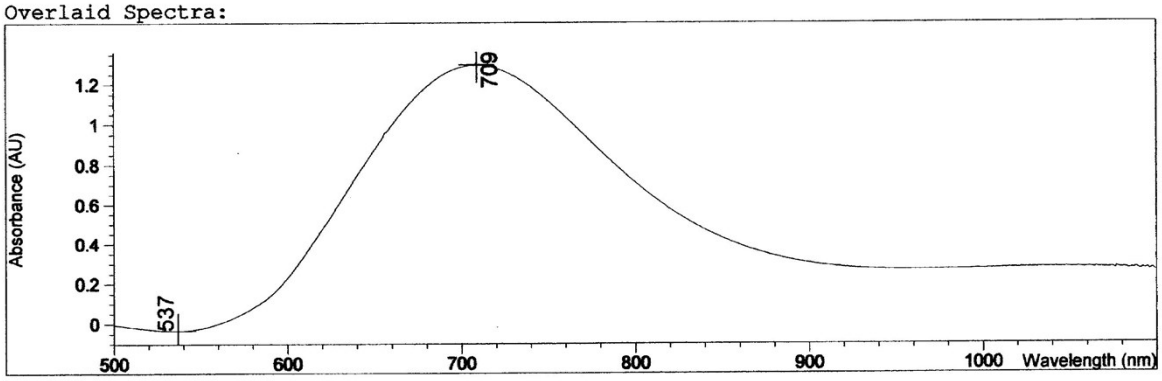
Fig. S33 ESI-MS of complex **5** in CH_3CN

Method file : TEST.M (modified) Last update: Date 5/3/2017 Time 3:25:34 PM

Information : Default Method

Data File : C:\HPCHEM\1\DATA\3126AN.SD Created : 5/3/17 15:21:19

Overlaid Spectra:



#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1		709.0	1.29580	537.0	-3.3723E-2

Fig. S34 Electronic spectrum of complex **5-PF_6** (4.411 x 10^{-3} M) in CH_3CN